

WEST Search History

DATE: Thursday, February 20, 2003

Set Name Query

side by side

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result set

DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR

L15	114 and alpha adj 2 adj macroglobulin adj receptor	16	L15
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L14	L13 and immune near5 response	1153	L14
-----	-------------------------------	------	-----

L13	heat adj shock adj protein and fragment\$	2713	L13
-----	---	------	-----

L12	alpha adj 2 adj macroglobulin adj receptor and tissue adj type adj plasminogen adj activator	4	L12
-----	--	---	-----

DB=USPT; PLUR=YES; OP=OR

L11	110 and alpha adj 2 adj macroglobulin adj receptor	1	L11
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L10	6239106.pn.	1	L10
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DB=EPAB; PLUR=YES; OP=OR

L9	WO009950303A2	1	L9
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DB=USPT,PGPB; PLUR=YES; OP=OR

L8	5639876.pn.	1	L8
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L7	L5 and heat adj shock adj protein	1	L7
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L6	L5 and heat shock protein	293476	L6
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L5	6403080.pn.	1	L5
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L4	heat adj shock adj protein and alpha adj 2 adj macroglobulin	61	L4
----	--	----	----

L3	heat adj shock adj protein near10 alpha adj 2 adj macroglobulin	2	L3
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L2	heat adj shock adj protein near10 cd91	0	L2
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L1	modulat\$ and heat adj shock adj protein near10 cd91	0	L1
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END OF SEARCH HISTORY

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NEWS 3 Apr 09 BELSTEIN: Reload and implementation of a New Subject Area
NEWS 4 Apr 09 ZDB will be removed from STN
NEWS 5 Apr 19 US Patent Applications available in IFICDB, IFIPAT, and IFIUDS
NEWS 6 Apr 22 Records from IP.com available in CAPUS, HCAPUS, and ZCAPUS
NEWS 7 Apr 22 BIOSIS Gene Names now available in TOXCENTER
NEWS 8 Apr 22 Federal Research in Progress (FEDRIP) now available
NEWS 9 Jun 03 New e-mail delivery for search results now available
NEWS 10 MEDLINE Reload
NEWS 11 Jun 10 PCTFUL has been reloaded
NEWS 12 Jul 02 FORGE no longer contains STANDARDS file segment
NEWS 13 Jul 22 USAN to be reloaded July 28, 2002;
NEWS 14 Jul 29 saved answer sets no longer valid
NEWS 15 Jul 30 ENHANCED polymer searching in REGISTRY
NEWS 16 Aug 08 NETFIRST to be removed from STN
NEWS 17 Aug 08 PHARMARKETLETT(PharmAml) - new on STN
NEWS 18 Aug 08 NTIS has been reloaded and enhanced
NEWS 19 Aug 19 Aquatic Toxicity Information Retrieval (AQUIRE)
NEWS 20 Aug 19 now available on STN
NEWS 21 Aug 19 IFIPAT, IFICDB, and IFIUDS have been reloaded
NEWS 22 Aug 19 The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 23 Sep 03 Sequence searching in REGISTRY enhanced
NEWS 24 Sep 03 JAPIO has been reloaded and enhanced
NEWS 25 Sep 16 Experimental properties added to the REGISTRY file
NEWS 26 Oct 01 CA Section Thesaurus available in CAPUS and CA
NEWS 27 Oct 21 CASREACT Enriched with reactions from 1907 to 1985
NEWS 28 Oct 24 BELSTEIN adds new search fields
NEWS 29 Oct 24 Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 30 Oct 25 MEDLINE SDI run of October 8, 2002
NEWS 31 Nov 18 DKILIT has been renamed APOILIT
NEWS 32 Dec 02 More calculated properties added to REGISTRY
NEWS 33 Dec 02 TIBKAT will be removed from STN
NEWS 34 Dec 04 CSA files on STN
NEWS 35 Dec 17 PCTFUL now covers WP/PCT Applications from 1978 to date
NEWS 36 Dec 17 TOXCENTER enhanced with additional content
NEWS 37 Dec 17 Adis Clinical Trials Insight now available on STN
NEWS 38 Dec 30 ISMEC no longer available
NEWS 39 Jan 13 Indexing added to some pre-1967 records in CA/CAPUS
NEWS 40 Jan 21 NUTRACEUT offering one free connect hour in February 2003
NEWS 41 Jan 21 PHARMAML offering one free connect hour in February 2003
NEWS 42 Jan 29 Simultaneous left and right truncation added to COMPENDEX,
ENERGY, INSPEC
NEWS 43 Feb 13 CANCERLIT is no longer being updated
NEWS EXPRESS January 6 CURRENT WINDOWS VERSION IS V6.01a,
CURRENT MACINTOSH VERSION IS V6.0b(ENGL) AND V6.0db(JP).

AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
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FILE 'HOME' ENTERED AT 15:25:49 ON 20 FEB 2003

=> file medicine, cancerlit, biosis, confaci, embase, caplus, uspatfull
COST IN U.S. DOLLARS SINCE FILE TOTAL
FULL ESTIMATED COST ENTRY SESSION
0.21 0.21

FILE 'MEDLINE' ENTERED AT 15:26:27 ON 20 FEB 2003

FILE 'CANCERLIT' ENTERED AT 15:26:27 ON 20 FEB 2003

FILE 'BIOSIS' ENTERED AT 15:26:27 ON 20 FEB 2003
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FILE 'USPATFULL' ENTERED AT 15:26:27 ON 20 FEB 2003
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

=> s heat (a) shock (a) protein
L1 72563 HEAT (A) SHOCK (A) PROTEIN

=> s 11 and alpha (a) 2 (a) macroglobulin (a) receptor
L2 40 L1 AND ALPHA (A) 2 (A) MACROGLOBULIN (A) RECEPTOR

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3 33 DUP REM L2 (7 DUPLICATES REMOVED)

=> d 1-33 lbib

L3 ANSWER 1 OF 33 USPATFULL
ACCESSION NUMBER: 2003:40533 USPATFULL
TITLE: Methods for the inhibition of epstein-barr virus
transmission employing anti-viral peptides capable of
abrogating viral fusion and transmission
Barney, Shawn O'lin, Cary, NC, United States
Lambert, Dennis Michael, Cary, NC, United States

INVENTOR(S):

PATENT ASSIGNEE(S) :
Petteway, Stephen Robert, Cary, NC, United States
Trimeris, Inc., Durham, NC, United States (U.S.
corporation)

PATENT INFORMATION:
US 6518013 B1 20030211
US 1995-485546 19950607 (8)
Continuation-in-part of Ser. No. US 1994-360107, filed
on 20 Dec 1994, now patented, Pat. No. US 6017536
Continuation-in-part of Ser. No. US 1994-255208, filed
on 7 Jun 1994 Continuation-in-part of Ser. No. US
1993-73028, filed on 7 Jun 1993, now patented, Pat. No.
US 5464933

DOCUMENT TYPE:
FILE SEGMENT:
PRIMARY EXAMINER:
ASSISTANT EXAMINER:
LEGAL REPRESENTATIVE:
NUMBER OF CLAIMS:
EXEMPLARY CLAIM:
NUMBER OF DRAWINGS:
LINE COUNT:
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 2 OF 33 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER:
DOCUMENT NUMBER:
TITLE:

INVENTOR(S) :
PATENT ASSIGNEE(S) :
SOURCE:
DOCUMENT TYPE:
LANGUAGE:
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE
WO 2002022886 A2 20020321 WO 2001-US29096 20010918
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GR, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TW, TR, TT, TZ, UA, UG, UZ,
VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RM: GH, GM, KE, LS, MW, WZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MD, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GN, IQ, GM, NI, MR, SN, TD, TG
AU 2001091059 A5 20020326 20010918
US 2003013093 A1 20030116 US 2001-955367 20010918
US 2000-23339P P 20000918
PRIORITY APPLN. INFO.:
WO 2001-US29096 W 20010918

L3 ANSWER 3 OF 33 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER:
DOCUMENT NUMBER:
TITLE:
INVENTOR(S) :
Laukkonen, Mattias; Moses, Ashlee; Fusch, Klaus;

PATENT ASSIGNEE(S) :
Nelson, Jay; Bell, Yolanda; Heinrich, Michael; Simmen,
Kenneth
Orcho-McNeil Pharmaceutical, Inc., USA; Oregon Health
& Science University
PCT Int. Appl., 95 pp.
CODEN: PIXXD2

DOCUMENT TYPE:
LANGUAGE:
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE
WO 2002010339 A2 20020207 WO 2001-US24469 20010801
WO 2002010339 A3 20020404
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GR, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TW, TR, TT, TZ, UA, UG, UZ,
VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RM: GH, GM, KE, LS, MW, WZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MD, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GN, IQ, GM, NI, MR, SN, TD, TG
US 2000-222162P P 20000802
PRIORITY APPLN. INFO.:

L3 ANSWER 4 OF 33 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER:
DOCUMENT NUMBER:
TITLE:

INVENTOR(S) :
PATENT ASSIGNEE(S) :
SOURCE:
DOCUMENT TYPE:
LANGUAGE:
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE
JP 2002355079 A2 20021210 JP 2002-69354 20020313
JP 2001-73183 A 20010314
JP 2001-74993 A 20010315
JP 2001-102519 A 20010330
PRIORITY APPLN. INFO.:

L3 ANSWER 5 OF 33 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER:
TITLE:
INVENTOR(S) :
Ternan, David S., Pebble Beach, CA, UNITED STATES

PATENT INFORMATION:
APPLICATION INFO.:
PRIORITY INFORMATION:
DOCUMENT TYPE:
FILE SEGMENT:

LEGAL REPRESENTATIVE: David S. Terman, P.O. Box 987, Pebble Beach, CA, 93953
NUMBER OF CLAIMS: 30
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Page(s)
LINE COUNT: 17323
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 6 OF 33 USPATFULL
ACCESSION NUMBER: 2002:259381 USPATFULL
TITLE: Materials and methods relating to lipid metabolism
INVENTOR(S): Ballinger, Dennis G., Menlo Park, CA, UNITED STATES
Loeb, Deborah, San Jose, CA, UNITED STATES
Montgomery, Julie R., Santa Cruz, CA, UNITED STATES
Tang, Y. Tom, San Jose, CA, UNITED STATES
Zhou, Ping, Cupertino, CA, UNITED STATES
Goodrich, Kyle, San Jose, CA, UNITED STATES
Liu, Chenghua, San Jose, CA, UNITED STATES
Asundi, Vinod, Foster City, CA, UNITED STATES
Zhao, Qing A., San Jose, CA, UNITED STATES
Wehrman, Tom, Stanford, CA, UNITED STATES
Dranac, Radoje T., Palo Alto, CA, UNITED STATES
Ren, Feiyan, Cupertino, CA, UNITED STATES
Qian, Xiaohong B., San Jose, CA, UNITED STATES
Mang, Dunxui, Poway, CA, UNITED STATES

PATENT INFORMATION: US 2002:42853 A1 2002:1003
APPLICATION INFO.: US 2001-83596 A1 2001:0416 (9)
RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2000-714936, filed on 17 Nov 2000, PENDING Continuation-in-part of Ser. No. US 2000-667298, filed on 22 Sep 2000, PENDING Continuation-in-part of Ser. No. US 2000-631451, filed on 3 Aug 2000, PENDING Continuation-in-part of Ser. No. US 2000-598042, filed on 20 Jun 2000, PENDING

NUMBER	KIND	DATE
US 2000-197137P	2000:0414 (60)	

PRIORITY INFORMATION: US 2000-197137P 2000:0414 (60)
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MARSHALL, GERSTEIN & BORUN, 6300 SEARS TOWER, 233 SOUTH WACKER, CHICAGO, IL, 60606-6357
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 30 Drawing Page(s)
LINE COUNT: 9120
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 7 OF 33 USPATFULL
ACCESSION NUMBER: 2002:206116 USPATFULL
TITLE: Toxicant-induced differential gene expression
INVENTOR(S): Reithaar-Olson, John F., Montclair, NJ, UNITED STATES

NUMBER	KIND	DATE
US 2002:110808	A1	2002:0815
US 2000-489220	A1	2000:0121 (9)

UTILITY
APPLICATION
VICKI G. NORTON, ESQ., BROBECK, PHLEGER AND HARRISON LLP, 12390 EL COMINO REAL, SAN DIEGO, CA, 92130
NUMBER OF CLAIMS: 28
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Page(s)

LINE COUNT: 5161
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 8 OF 33 USPATFULL
ACCESSION NUMBER: 2002:164658 USPATFULL
TITLE: Immunotherapeutic methods for extracorporeal modulation of CD36 and its ligands
INVENTOR(S): Srivastava, Pramod K., Avon, CT, UNITED STATES

NUMBER	KIND	DATE
US 2002:086276	A1	2002:0704
US 2000-750973	A1	2000:1228 (9)

UTILITY
APPLICATION
PENNIE AND EDMONDS, 1155 AVENUE OF THE AMERICAS, NEW YORK, NY, 100362711
NUMBER OF CLAIMS: 19
EXEMPLARY CLAIM: 1
LINE COUNT: 1813
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 9 OF 33 USPATFULL
ACCESSION NUMBER: 2002:66639 USPATFULL
TITLE: Compositions comprising heat shock proteins or alpha(2) macroglobulin, antigenic molecules and saponins, and methods of use thereof
INVENTOR(S): Armen, Garo H., Mahanaset, NY, UNITED STATES

NUMBER	KIND	DATE
US 2002:037290	A1	2002:0328
US 2001-909778	A1	2001:0720 (9)

PATENT INFORMATION: US 2000-223133P 2000:0807 (60)
APPLICATION INFO.: Utility
RELATED APPLN. INFO.: APPLICATION
LEGAL REPRESENTATIVE: Pennie & Edmonds LLP, 1155 Avenue of the Americas, New York, NY, 10036-2711
NUMBER OF CLAIMS: 119
EXEMPLARY CLAIM: 1
LINE COUNT: 4136
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 10 OF 33 USPATFULL
ACCESSION NUMBER: 2002:48016 USPATFULL
TITLE: Complexes of alpha (2) macroglobulin and antigenic molecules for immunotherapy
INVENTOR(S): Srivastava, Pramod K., Avon, CT, UNITED STATES

NUMBER	KIND	DATE
US 2002:028207	A1	2002:0307
US 2001-873403	A1	2001:0604 (9)

UTILITY
APPLICATION
PENNIE AND EDMONDS, 1155 AVENUE OF THE AMERICAS, NEW YORK, NY, 100362711
NUMBER OF CLAIMS: 28
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Page(s)

YORK, NY, 100362711

NUMBER OF CLAIMS: 36
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 65 Drawing Page(s)
LINE COUNT: 4477
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 11 OF 33 USPTAFULL
ACCESSION NUMBER: 2002:297296 USPTAFULL
TITLE: Methods for inhibition of membrane fusion-associated events, including respiratory syncytial virus transmission
INVENTOR(S): Bolognesi, Dani Paul, Durham, NC, United States
Matthews, Thomas James, Durham, NC, United States
Wild, Carl T., Durham, NC, United States
Barney, Shawn O'Lin, Cary, NC, United States
Lambert, Dennis Michael, Cary, NC, United States
Petteaway, Stephen Robert, Cary, NC, United States
Langlois, Alphonse J., Durham, NC, United States
Trimeris, Inc., Durham, NC, United States (U.S. corporation)

PATENT ASSIGNEE(S):

NUMBER KIND DATE
US 6479055 B1 20021112
US 1995-470896 19950606 (8)
Continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994, now patented, Pat. No. US 6017536
Continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994
Continuation-in-part of Ser. No. US 1993-73028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933
UTILITY GRANTED
DOCUMENT TYPE:
FILE SEGMENT:
LEGAL REPRESENTATIVE: Stucker, Jeffrey
Femite & Edmonds LLP
NUMBER OF CLAIMS: 44
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 84 Drawing Figure(s); 83 Drawing Page(s)
LINE COUNT: 26553
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 12 OF 33 USPTAFULL
ACCESSION NUMBER: 2002:136555 USPTAFULL
TITLE: Methods of modulating an immune response to antigen, and cells for use in the method
INVENTOR(S): Segal, Andrew H., Boston, MA, United States
PATENT ASSIGNEE(S): Whitehead Institute for Biomedical Research, Cambridge, MA, United States (U.S. corporation)

NUMBER KIND DATE
US 6403080 B1 20020611
US 1999-339523 19990624 (9)
Division of Ser. No. US 1997-826259, filed on 27 Mar 1997, now patented, Pat. No. US 5951976

NUMBER DATE
US 1996-14364P 19960328 (60)
UTILITY GRANTED
DOCUMENT TYPE:
FILE SEGMENT:
PRIMARY EXAMINER: Bansal, Geetha P.
LEGAL REPRESENTATIVE: Williams, Kathleen Madden, Palmer & Dodge, LLP
NUMBER OF CLAIMS: 25

EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 2153
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 13 OF 33 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:471412 CAPLUS
DOCUMENT NUMBER: 137:92694
TITLE: The endoplasmic reticulum-resident heat shock protein Grp96 activates dendritic cells via the toll-like receptor 2/4 pathway
AUTHOR(S): Vabulas, Ramunas M.; Braedel, Sibylla; Hile, Norbert; Singh-Jasuja, Harpreet; Hertter, Sylvia; Ahmad-Nejad, Parviz; Kirschning, Carsten J.; da Costa, Claressa; Ramaneese, Hans-Georg; Wagner, Hermann; Schild, Hansjorg
CORPORATE SOURCE: Institute for Medical Microbiology, Immunology and Hygiene, Technical University of Munich, Munich, D-81675, Germany
JOURNAL OF BIOLOGICAL CHEMISTRY (2002), 277(23), 20847-20853
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
JOURNAL
LANGUAGE: English
ENTRY MONTH: 35
THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 14 OF 33 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:899128 CAPLUS
DOCUMENT NUMBER: 138:88135
TITLE: Structure-function studies of the receptors for complement C1q
AUTHOR(S): McCreath, E.; Gaege, P.
CORPORATE SOURCE: University of Oxford, Sir William Dunn School of Pathology, Oxford, OX1 3RE, UK
JOURNAL OF BIOLOGICAL CHEMISTRY (2002), 277(6), 1010-1014
CODEN: BCBTBS; ISSN: 0300-5127
PUBLISHER: Portland Press Ltd.
JOURNAL: General Review
LANGUAGE: English
ENTRY MONTH: 50
THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 15 OF 33 MEDLINE MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2002051981
DOCUMENT NUMBER: 21636470 PubMed ID: 11777948
TITLE: The receptor for heat shock protein 60 on macrophages is saturable, specific, and distinct from receptors for other heat shock proteins.
AUTHOR: Habich-Christiane; Baumgart Karina; Kolb Hubert; Burkart Volker
CORPORATE SOURCE: German Diabetes Research Institute at the Heinrich-Heine-University of Dusseldorf, Dusseldorf, Germany..
JOURNAL OF IMMUNOLOGY, (2002 Jan 15) 168 (2) 569-76.
JOURNAL CODE: 2985117R. ISSN: 0022-1767.
United States
JOURNAL: Article: (JOURNAL ARTICLE)
LANGUAGE: English
ENTRY MONTH: 200201
Abridged Index Medicus Journals; Priority Journals

ENTRY DATE: Entered STN: 20020125
Last Updated on STN: 20020201
Entered Medicine: 20020131

L3 ANSWER 16 OF 33 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:183243 CAPLUS
DOCUMENT NUMBER: 136:308105
TITLE: Heat shock proteins 70
and 60 share common receptors which are expressed on
human monocyte-derived but not epidermal dendritic
cells

AUTHOR(S):

Lipkover, Dan; Ziyian, Umit; Spehner, Daniele; Proamer,
Fabienne; Bausinger, Hugues; Jeannin, Pascale;
Salameo, Jean; Bobbot, Alain; Cazenave, Jean-Pierre;
Drillien, Robert; Delneste, Yves; Hanau, Daniel; De la
Salle, Henri
INSERM, Equipe Propre 99-08, Etablissement Francais du
Sang - Alsace, Strasbourg, Fr.
European Journal of Immunology (2002), 32(12), 322-332
CODEN: EJIMAF; ISSN: 0014-2980
Wiley-VCH Verlag GmbH
Journal
English

PUBLISHER:
DOCUMENT TYPE:
LANGUAGE:
REFERENCE COUNT: 35
THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 17 OF 33 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:828415 CAPLUS
DOCUMENT NUMBER: 137:89412
TITLE: Detection of variations in the DNA methylation profile
of genes in the determining the risk of disease
Berlin, Kurt; Pispemrock, Christian; Olek, Alexander
Epigenomics A.-G., Germany
PCT Int. Appl., 636 pp.
CODEN: PIXXD2
Patent
German

DOCUMENT TYPE:
LANGUAGE:
FAMILY ACC. NUM. COUNT: 68
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE
WO 2001077373 A2 20011018 WO 2001-XA1486 20010406
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CR, CU, CZ, DK, DM, DE, EE, ES, FI, GB, GR, GU, HA, HE, HU,
ID, IL, IN, IS, JP, KE, KR, KZ, LC, LK, LR, LS, LT, LU,
LV, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI,
SE, SG, SI, SK, SL, ST, SV, TD, TH, TJ, TT, UA, UG, UZ, VN, YU, ZA,
ZM, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
CF, CG, CI, CM, CW, GA, GU, HT, KE, MG, ML, MR, NE, NG, TD, TG
DE 10019058 A1 20011220 DE 2000-10019058 20000406
WO 2001077373 A2 20011018 WO 2001-DE1486 20010406
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CR, CU, CZ, DK, DM, DE, EE, ES, FI, GB, GR, GU, HA, HE, HU,
ID, IL, IN, IS, JP, KE, KR, KZ, LC, LK, LR, LS, LT, LU,
LV, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI,
SE, SG, SI, SK, SL, ST, SV, TD, TH, TJ, TT, UA, UG, UZ, VN, YU, ZA,
ZM, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
CF, CG, CI, CM, CW, GA, GU, HT, KE, MG, ML, MR, NE, NG, TD, TG
EP 1274865 A2 20030115 EP 2001-953936 20010406
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRIORITY APPLN. INFO.:

DE 2000-10019058 A 20000406
WO 2001-DE1486 W 20010406
DE 2000-10019173 A 20000407
DE 2000-10012529 A 20000610
DE 2000-10043826 A 20000901
WO 2001-EP3969 W 20010406

L3 ANSWER 18 OF 33 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:886449 CAPLUS
DOCUMENT NUMBER: 136:36328
TITLE: Alpha 2 macroglobulin
receptors as a heat shock
protein receptor and uses thereof

INVENTOR(S):
PATENT ASSIGNEE(S):
SOURCE: University of Connecticut Health Center, USA
PCT Int. Appl., 236 pp.
CODEN: PIXXD2
Patent
English

DOCUMENT TYPE:
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE
WO 2001092474 A1 20011206 WO 2001-US18041 20010604
W: AU, CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, TR

PRIORITY APPLN. INFO.:

US 2000-2090959 P 20000602
US 2000-625137 A 20000725
US 2000-668724 A 20000922
US 2000-750972 A 20001228
THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 19 OF 33 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:885810 CAPLUS
DOCUMENT NUMBER: 136:36322
TITLE: Complexes of .alpha.2-macroglobulin and antigenic
molecules for immunotherapy
Srivastava, Pramod K.
University of Connecticut Health Center, USA
PCT Int. Appl., 160 pp.
CODEN: PIXXD2
Patent
English

INVENTOR(S):
PATENT ASSIGNEE(S):
SOURCE: University of Connecticut Health Center, USA
PCT Int. Appl., 160 pp.
CODEN: PIXXD2
Patent
English

DOCUMENT TYPE:
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE
WO 2001091787 A1 20011206 WO 2001-US18047 20010604
W: AU, CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, TR

PRIORITY APPLN. INFO.:

US 2000-209266 P 20000602
US 2000-625139 A 20000725
THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 20 OF 33 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:851435 CAPLUS
DOCUMENT NUMBER: 136:1570
TITLE: Compositions, kits, and methods for identification and

INVENTOR(S) : modulation of T helper-1 and T helper-2 cells and diseases associated therewith
Hanshan, Catherine F.; Feldman, Marc; Tripicchio, William L.
PATENT ASSIGNEE(S) : Genetics Institute, Inc., USA; Kennedy Institute of Rheumatology
PCT Int. Appl., 115 pp.
SOURCE :
DOCUMENT TYPE : Patent
LANGUAGE : English
FAMILY ACC. NUM. COUNT : 1
PATENT INFORMATION :
CODEN: PIXXD2

PATENT NO. : 2001088199
KIND : A2
DATE : 20011122
APPLICATION NO. : 2001-088199
DATE : 20010517
W : AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GR, GU, HK, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, LU, MA, MD, MG, MK, MN, MW, MX, MY, NZ, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW : GH, GM, KE, LS, MM, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GN, GW, ML, MR, NE, NI, TD, TG, US 2002039734 A1 20020404 US 2001-860655 20010517
PRIORITY APPL. INFO : US 2000-205204P P 20000518

L3 ANSWER 21 OF 33 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER : 2001.676999 CAPLUS
DOCUMENT NUMBER : 135:252790
TITLE : Single nucleotide polymorphisms in human genes
INVENTOR(S) : Cargill, Michele; Ireland, James S.; Lander, Eric S.
PATENT ASSIGNEE(S) : Whitehead Institute for Biomedical Research, USA
SOURCE : PCT Int. Appl., 145 pp.
CODEN: PIXXD2

DOCUMENT TYPE : Patent
LANGUAGE : English
FAMILY ACC. NUM. COUNT : 1
PATENT INFORMATION :

PATENT NO. : 2001066800
KIND : A2
DATE : 20010913
APPLICATION NO. : 2001-066800
DATE : 20010307
W : AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GR, GU, HK, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, LU, MA, MD, MG, MK, MN, MW, MX, MY, NZ, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW : GH, GM, KE, LS, MM, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GN, GW, ML, MR, NE, NI, TD, TG, US 2002032319 A1 20020314 US 2001-801274 20010307
PRIORITY APPL. INFO : US 2000-187510P P 20000307
US 2000-206129P P 20000522

L3 ANSWER 22 OF 33 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER : 2001.319729 CAPLUS
DOCUMENT NUMBER : 134:320865
TITLE : Regulation of apob for diagnosis, treatment and drug screening for cardiovascular and metabolic disorders or syndromes
INVENTOR(S) : Fisher, Edward A.; Williams, Kevin Jon
PATENT ASSIGNEE(S) : Thomas Jefferson University, USA

SOURCE : PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE : Patent
LANGUAGE : English
FAMILY ACC. NUM. COUNT : 1
PATENT INFORMATION :

PATENT NO. : 2001030354
KIND : A1
DATE : 20010503
APPLICATION NO. : 2000-030354
DATE : 20001026
W : AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GR, GU, HK, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, LU, MA, MD, MG, MK, MN, MW, MX, MY, NZ, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW : GH, GM, KE, LS, MM, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GN, GW, ML, MR, NE, NI, TD, TG, US 1999-161537P P 19991026
PRIORITY APPL. INFO :
REFERENCE COUNT : 1
THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 23 OF 33 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER : 2001.67794 CAPLUS
DOCUMENT NUMBER : 135:252790
TITLE : Human respiratory syncytial virus peptides with anti-infective and antiviral activities
INVENTOR(S) : Barney, Shawn O.; Lin, Cary, NC, United States
PATENT ASSIGNEE(S) : Lambert, Dennis Michael, Cary, NC, United States
Pettey, Stephen Robert, Cary, NC, United States
Trimeris, Inc., Durham, NC, United States (U.S. corporation)

NUMBER : 1
KIND : B1
DATE : 20010508

PATENT INFORMATION :
APPLICATION INFO :
RELATED APPL. INFO :
US 6228983 B1 20010508
US 1995-485264 19950607 (b)
Division of Ser. No. US 1995-470896, filed on 6 Jun 1995
Continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994
Continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994
Continuation-in-part of Ser. No. US 1993-73028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933

DOCUMENT TYPE : Utility
FILE SEGMENT : Granted
PRIMARY EXAMINER : Schneider, Laurie
ASSISTANT EXAMINER : Parkin, Jeffrey S.
LEGAL REPRESENTATIVE : Pennie & Edmonds LLP
NUMBER OF CLAIMS : 62
EXEMPLARY CLAIMS :
1 84 Drawing Figure(s); 83 Drawing Page(s)
2 32166
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 24 OF 33 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER : 2001.286503 CAPLUS
DOCUMENT NUMBER : 135:136110
TITLE : Adjuvant activity of .alpha.2-macroglobulin, an independent ligand for the heat shock protein receptor CD91
INVENTOR(S) : Binder, Robert J.; Karimeddini, David; Srivastava, Pramod K.
CORPORATE SOURCE : Center for Immunotherapy of Cancer and Infectious Diseases, University of Connecticut School of Medicine, Farmington, CT, 06030, USA

SOURCE: Journal of Immunology (2001), 166(8), 4968-4972
 PUBLISHER: American Association of Immunologists
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 REFERENCE COUNT: 14
 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 25 OF 33 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2001:782994 CAPLUS
 DOCUMENT NUMBER: 136:68297
 TITLE: To find the road traveled to tumor immunity: the trafficking itineraries of molecular chaperones in antigen-presenting cells
 AUTHOR(S): Berwin, B.; Nicchitta, C. V.
 CORPORATE SOURCE: Department of Cell Biology, Duke University Medical Center, Durham, NC, 27710, USA
 SOURCE: Traffic (Copenhagen, Denmark) (2001), 2(10), 690-697
 PUBLISHER: Travepa; ISSN: 1398-9219
 DOCUMENT TYPE: Munksgaard International Publishers Ltd.
 LANGUAGE: Journal; General Review
 REFERENCE COUNT: 41
 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 26 OF 33 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2001:263289 CAPLUS
 DOCUMENT NUMBER: 135:32507
 TITLE: CD91 is a common receptor for heat shock proteins gp96, hsp90, hsp70, and calreticulin
 AUTHOR(S): Basu, Sreyashi; Binder, Robert J.; Ramalingam, Thirumalai; Srivastava, Pramod K.
 CORPORATE SOURCE: Center for Immunotherapy of Cancer and Infectious Diseases, University of Connecticut School of Medicine, Farmington, CT, 06030, USA
 SOURCE: Immunity (2001), 14(3), 303-313
 PUBLISHER: Immunity; ISSN: 1074-7613
 DOCUMENT TYPE: Cell Press
 LANGUAGE: Journal
 REFERENCE COUNT: 34
 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 27 OF 33 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2001:361126 CAPLUS
 DOCUMENT NUMBER: 135:150447
 TITLE: Differential expression of multiple genes during articular chondrocyte redifferentiation
 AUTHOR(S): Haudenschild, Dominik R.; McPherson, John M.; Tubo, Ross; Binette, Francois
 CORPORATE SOURCE: Genzyme Tissue Repair, Framingham, MA, USA
 SOURCE: Anatomical Record (2001), 263(1), 91-98
 PUBLISHER: Anatomical Record; ISSN: 0003-276X
 DOCUMENT TYPE: Wiley-Liss, Inc.
 LANGUAGE: Journal
 REFERENCE COUNT: 36
 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 28 OF 33 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2000:759895 CAPLUS
 DOCUMENT NUMBER: 134:28172
 TITLE: The expression of adipogenic genes is decreased in obesity and diabetes mellitus

AUTHOR(S): Nadler, Samuel T.; Stoeck, Jonathan P.; Schueler, Kathryn L.; Tanimoto, Gene; Yandell, Brian S.; Attie, Alan D.
 CORPORATE SOURCE: Department of Biochemistry, University of Wisconsin, Madison, WI, 53706, USA
 SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2000), 97(21), 11371-11376
 PUBLISHER: PNAS; ISSN: 0027-8424
 DOCUMENT TYPE: National Academy of Sciences
 LANGUAGE: Journal
 REFERENCE COUNT: 40
 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 29 OF 33 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2000:908423 CAPLUS
 DOCUMENT NUMBER: 134:203644
 TITLE: Morphologic analysis correlates with gene expression changes in cultured F344 rat mesothelial cells
 AUTHOR(S): Crosby, L. M.; Hyder, K. S.; DeAngelis, A. B.; Keppler, T. B.; Gaskill, B.; Benavides, G. R.; Yoon, L.; Morgan, K. T.
 CORPORATE SOURCE: University of North Carolina at Chapel Hill, Curriculum in Toxicology/U.S. EPA NHEERL, Research Triangle Park, NC, 27711, USA
 SOURCE: Toxicology and Applied Pharmacology (2000), 169(3), 205-221
 PUBLISHER: Academic Press
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 REFERENCE COUNT: 60
 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 30 OF 33 MEDLINE MEDLINE
 ACCESSION NUMBER: 2001216038
 DOCUMENT NUMBER: 21205395
 TITLE: CD91: a receptor for heat shock protein gp96.
 COMMENT: Comment in: Nat Immunol. 2000 Aug;1(2):100-1
 AUTHOR: Binder R J; Han D K; Srivastava P K
 CORPORATE SOURCE: Center for Immunotherapy of Cancer and Infectious Diseases, University of Connecticut School of Medicine, Farmington, CT 06030, USA.
 CONTRACT NUMBER: CA64394 (NCI)
 SOURCE: Nat Immunol. (2000 Aug) 1 (2) 151-5.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200105
 ENTRY DATE: Entered STM: 20010521
 Last Updated on STM: 20010521
 Entered Medline: 20010517

L3 ANSWER 31 OF 33 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 1999:795994 CAPLUS
 DOCUMENT NUMBER: 132:31744
 TITLE: Gene probes used for genetic profiling in healthcare screening and planning
 INVENTOR(S): Roberts, Gareth Wyn
 PATENT ASSIGNEE(S): Genosic Pharma Ltd., UK
 SOURCE: PCT Int. Appl., 745 pp.

DOCUMENT TYPE: CODEN: PIXXD2
LANGUAGE: Patent
FAMILY ACC. NUM. COUNT: 2 English
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 19964627	A2	19991216	WO 1999-GB1780	19990604
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TU, TM				
RM: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPL. INFO.:
GB 1998-12099 A 19980606
GB 1998-13291 A 19980620
GB 1998-13611 A 19980624
GB 1998-13835 A 19980627
GB 1998-14110 A 19980701
GB 1998-14580 A 19980707
GB 1998-15438 A 19980716
GB 1998-15574 A 19980718
GB 1998-15576 A 19980718
GB 1998-15576 A 19980718
GB 1998-16085 A 19980724
GB 1998-16086 A 19980724
GB 1998-16921 A 19980805
GB 1998-17097 A 19980807
GB 1998-17200 A 19980808
GB 1998-17632 A 19980814
GB 1998-17943 A 19980819

L3 ANSWER 33 OF 33 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 19991795993 CAPLUS
DOCUMENT NUMBER: 132:31743
TITLE: Gene probes used for genetic profiling in healthcare screening and planning
INVENTOR(S): Roberts, Gareth Wyn
PATENT ASSIGNEE(S): Genosic Pharma Limited, UK
SOURCE: PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 19964626	A2	19991216	WO 1999-GB1779	19990604
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TU, TM				
RM: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

AU 9941586 A1 19991230 AU 1999-41586 19990604
AU 9941587 A1 19991230 AU 1999-41587 19990604
GB 2339200 B2 20010912 GB 1999-12914 19990604
GB 2339200 B2 20010912

EP 1084273 A1 20010321 EP 1999-925207 19990604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
PRIORITY APPL. INFO.:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 19964627	A2	19991216	WO 1999-GB1780	19990604
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TU, TM				
RM: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPL. INFO.:
GB 1998-12099 A 19980606
GB 1998-13291 A 19980620
GB 1998-13611 A 19980624
GB 1998-13835 A 19980627
GB 1998-14110 A 19980701
GB 1998-14580 A 19980707
GB 1998-15438 A 19980716
GB 1998-15574 A 19980718
GB 1998-15576 A 19980718
GB 1998-15576 A 19980718
GB 1998-16085 A 19980724
GB 1998-16086 A 19980724
GB 1998-16921 A 19980805
GB 1998-17097 A 19980807
GB 1998-17200 A 19980808
GB 1998-17632 A 19980814
GB 1998-17943 A 19980819
WO 1999-GB1779 W 19990604

L3 ANSWER 33 OF 33 USPTFULL
ACCESSION NUMBER: 1999141305 USPTFULL
TITLE: Adjuvant for transcutaneous immunization
INVENTOR(S): Glenn, Gregory M., Bethesda, MD, United States
Alving, Carl R., Bethesda, MD, United States
The United States of America as represented by the U.S. Army Medical Research & Materiel Command, Washington, DC, United States (U.S. government)
PATENT ASSIGNEE(S):
PATENT INFORMATION:
APPLICATION INFO.: US 5980898 19991109
RELATED APPL. INFO.: US 1997-896085 19970717 (8)
Continuation-in-part of Ser. No. US 1996-749164, filed on 14 Nov 1996
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Saunders, David
ASSISTANT EXAMINER: Tung, Mary Beth
LEGAL REPRESENTATIVE: Pillsbury, Madison & Suto LLP
NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1. 11
NUMBER OF DRAWINGS: 1
DRAWING FIGURE(S): 5 Drawing Page(s)
LINE COUNT: 1986
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d kwic 33

L3 ANSWER 33 OF 33 USPTFULL
ACCESSION NUMBER: 1999141305 USPTFULL
TITLE: Adjuvant for transcutaneous immunization
INVENTOR(S): Glenn, Gregory M., Bethesda, MD, United States
Alving, Carl R., Bethesda, MD, United States
The United States of America as represented by the U.S. Army Medical Research & Materiel Command, Washington, DC, United States (U.S. government)
PATENT ASSIGNEE(S):
PATENT INFORMATION:
APPLICATION INFO.: US 5980898 19991109
RELATED APPL. INFO.: US 1997-896085 19970717 (8)
Continuation-in-part of Ser. No. US 1996-749164, filed on 14 Nov 1996
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Saunders, David
ASSISTANT EXAMINER: Tung, Mary Beth
LEGAL REPRESENTATIVE: Pillsbury, Madison & Suto LLP
NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1. 11
NUMBER OF DRAWINGS: 1
DRAWING FIGURE(S): 5 Drawing Page(s)
LINE COUNT: 1986
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DET D Granulocyte-macrophage colony stimulating factor (reviewed in Nohria and Rubin, 1994), a muramyl dipeptide derivative (e.g., murabutide, threonyl-MDP or muramyl tripeptide), a heat shock protein or a derivative of Leishmania major Lel (Skelky et al., 1995), cholera toxin or cholera toxin B, a

Optionally, an activator of Langerhans cells may be used as an adjuvant. Examples of such activators include: inducers of heat shock protein; contact sensitizers (e.g., trinitrochlorobenzene, dinitrofluorobenzene, nitrogen mustard, pentadecylcatechol); toxins (e.g., Shiga toxin, Staph enterotoxin B); lipopolysaccharides, lipid A, or derivatives. amino acid peptide with A and B domains on the same peptide and binds to an entirely different receptor, the .alpha.2 -macroglobulin receptor/low density lipoprotein receptor-related protein (Kounnas et al., 1992). Despite the dissimilarities between ETA and CT in size, structure, and binding.

=> d kwic 12

L3 ANSWER 12 OF 33 USPATFULL
SUMM
TABLE 1
Exemplary Opsonin, APC binding moiety/APC receptor pairs useful according to the invention.
Opsonin Moiey Receptor
-alpha.-2 macroglobulin Val(1299)-Ala(1451) of human .alpha.-2 m receptor
C3b 42 N-terminal amino acids CRI of the .alpha.' chain of human C3b
C3b
SUMM
... bacilli bacterial antigens such as lipopolysaccharides and other gram-negative bacterial antigen components; Mycobacterium tuberculosis bacterial antigens such as mycolic acid, heat shock protein 65 (HSP65), the 30kDa major secreted protein, antigen 85A and other mycobacterial antigen components; Helicobacter pylori bacterial antigen components; pneumococcal . . . and methods of the invention include, but are not limited to, candida fungal antigen components; histoplasma fungal antigens such as heat shock protein 60 (HSP60) and other . . . histoplasma fungal antigen components; cryptococcal fungal antigens such as capsular polysaccharides and other cryptococcal fungal antigen. . .
SUMM
=> his
HIS IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system. For a list of commands available to you in the current file, enter "HELP COMMANDS" at an arrow prompt (=>).
=> d his
(FILE 'HOME' ENTERED AT 15:25:49 ON 20 FEB 2003)
FILE 'MEDLINE, CANCERLIT, BIOSIS, CONFSCI, EMBASE, CAPLUS, USPATFULL' ENTERED AT 15:26:27 ON 20 FEB 2003
L1 72563 S HEAT (A) SHOCK (A) PROTEIN
L2 40 S L1 AND ALPHA (A) 2 (A) MACROGLOBULIN (A) RECEPTOR
L3 33 DUP REM L2 (7 DUPLICATES REMOVED)
=> s l1 and antibody?
L4 12721 L1 AND ANTIBOD?
=> s l4 abd l2
MISSING OPERATOR L4 ABD
The search profile that was entered contains terms or nested terms that are not separated by a logical operator.
L5 => s l4 and l2
21 L4 AND L2
=> dup rem l5
PROCESSING COMPLETED FOR L5
L6 19 DUP REM L5 (2 DUPLICATES REMOVED)
=> d 1-19
L6 ANSWER 1 OF 19 USPATFULL
AN 2003:40533 USPATFULL
TI Methods for the inhibition of Epstein-Barr virus transmission employing

IN anti-viral peptides capable of abrogating viral fusion and transmission
Barney, Shawn O'lin, Gary, NC, United States
Lambert, Dennis Michael, Gary, NC, United States
Patteway, Stephen Robert, Gary, NC, United States
PA 6516013 B1 20030211 19950607 (8)
AI US 1995-485546
RLI Continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994, now patented, Pat. No. US 6017536 Continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994 Continuation-in-part of Ser. No. US 1993-73028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933
DT Utility
FS GRANTED
LN CNT 24700
INCL INCLM: 435/005.000 530/300.000; 530/324.000; 530/325.000; 530/326.000
NCL INCLM: 424/230.100; 530/300.000; 530/324.000; 530/325.000; 530/326.000
NCLM: 435/005.000
NLS: 424/230.100; 530/300.000; 530/324.000; 530/325.000; 530/326.000
IC ICM: C12Q001-70
EXF 435/5: 530/300; 530/324-329; 530/350; 424/230.1
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L6 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2002:937303 CAPLUS
DN 138:20443
TI Endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes
IN Kondo, Akihito, Takeda, Takeshi; Mizutani, Shigetoshi; Tsujimoto, Yoshinasa; Takashima, Ryokichi; Enoki, Yuki; Kato, Ikunoshin
PA Takara Bio Inc., Japan
SO Jpn. Kokai Tokyo Koho, 386 pp.
DT Patent
LA Japanese
LAJ Japanese
FAN CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE
PI JP 2002355079 A2 20021210 JP 2002-69354 20020313
PRAI JP 2001-73183 A 20010314
JP 2001-74993 A 20010315
JP 2001-102519 A 20010330
L6 ANSWER 3 OF 19 USPATFULL
AN 2002:315069 USPATFULL
TI Compositions and methods for treatment of neoplastic disease
IN Terman, David S., Reddie Beach, CA, UNITED STATES
PI US 2002177551 A1 20021128
AI US 2001-870759 A1 20010530 (9)
PRAI US 2000-208128P 20000531 (60)
DT Utility
FS APPLICATION
LN CNT 17323
INCL INCLM: 514/012.000
NCL INCLM: 435/325.000; 530/350.000
NCLM: 514/012.000
NLS: 435/325.000; 530/350.000
IC ICM: A61K038-17
ICS: C12N005-06; C07K014-705
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L6 ANSWER 4 OF 19 USPATFULL
AN 2002:259381 USPATFULL
TI Materials and methods relating to lipid metabolism

IN Ballinger, Dennis G., Menlo Park, CA, UNITED STATES
 Loeb, Deborah, San Jose, CA, UNITED STATES
 Montgomery, Julie R., Santa Cruz, CA, UNITED STATES
 Tang, Y. Tom, San Jose, CA, UNITED STATES
 Zhou, Ping, Cupertino, CA, UNITED STATES
 Goodrich, Ryle, San Jose, CA, UNITED STATES
 Liu, Chenghua, San Jose, CA, UNITED STATES
 Asundi, Vinod, Foster City, CA, UNITED STATES
 Zhao, Qing A., San Jose, CA, UNITED STATES
 Wehman, Tom, Stanford, CA, UNITED STATES
 Drmanac, Radolje T., Palo Alto, CA, UNITED STATES
 Ren, Feiyan, Cupertino, CA, UNITED STATES
 Qian, Xiaohong B., San Jose, CA, UNITED STATES
 Wang, Dunru, Poway, CA, UNITED STATES
 PI US 2002142953 AI 20021003
 US 2001-815996 AI 20010416 (9)
 RLI Continuation-in-part of Ser. No. US 2000-714936, filed on 17 Nov 2000,
 PENDING Continuation-in-part of Ser. No. US 2000-667296, filed on 22 Sep
 2000, PENDING Continuation-in-part of Ser. No. US 2000-631451, filed on
 3 Aug 2000, PENDING Continuation-in-part of Ser. No. US 2000-598042,
 filed on 20 Jun 2000, PENDING
 PRAI US 2000-197137P 20000414 (60)
 DT Utility
 FS APPLICATION
 LN.CNT 9120
 INCL INCLM: 514/012.000
 INCLS: 435/069.100; 435/325.000; 435/320.100; 530/359.000; 435/196.000;
 NCLM: 514/012.000
 NCL: 435/069.100; 435/325.000; 435/320.100; 530/359.000; 435/196.000;
 IC [7]
 ICM: A61K038-17
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 L6 ANSWER 5 OF 19 USPATFILL
 AN 2002:206116 USPATFILL
 TI Toxicant-induced differential gene expression
 IN Reichart-Olson, John F., Montclair, NJ, UNITED STATES
 PI US 2002110808 AI 20020815
 DT US 2000-489220 AI 20000121 (9)
 FS Utility
 FS APPLICATION
 LN.CNT 5161
 INCL INCLM: 435/006.000
 INCLS: 435/091.200; 536/023.100
 NCLM: 435/006.000
 NCL: 435/091.200; 536/023.100
 IC [7]
 ICM: C12Q001-68
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 L6 ANSWER 6 OF 19 USPATFILL
 AN 2002:164658 USPATFILL
 TI Immunotherapeutic methods for extracorporeal modulation of CD36 and its
 ligands
 IN Sriastava, Pramod K., Avon, CT, UNITED STATES
 PI US 2002086276 AI 20020704
 DT US 2000-750973 AI 20001228 (9)
 FS Utility
 FS APPLICATION
 LN.CNT 1813
 INCL INCLM: 435/002.000

NCL INCLS: 424/140.100
 NCLM: 435/002.000
 NCLS: 424/140.100
 IC [7]
 ICM: A61K039-395
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 L6 ANSWER 7 OF 19 USPATFILL
 AN 2002:66639 USPATFILL
 TI Compositions comprising heat shock proteins
 or alpha(2) macroglobulin, antigenic molecules and saponins, and methods
 of use thereof
 IN Armen, Garo H., Manhasset, NY, UNITED STATES
 PI US 2002037290 AI 20020328
 DT US 2001-909778 AI 20010720 (9)
 PRAI US 2000-223133P 20000807 (60)
 FS Utility
 FS APPLICATION
 LN.CNT 4136
 INCL INCLM: 424/178.100
 INCLS: 514/012.000; 514/026.000
 NCLM: 424/178.100
 NCL: 514/012.000; 514/026.000
 IC [7]
 ICM: A61K039-395
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 L6 ANSWER 8 OF 19 USPATFILL
 AN 2002:48016 USPATFILL
 TI Complexes of alpha (2) macroglobulin and antigenic molecules for
 immunotherapy
 IN Srivastava, Pramod K., Avon, CT, UNITED STATES
 PI US 2002028207 AI 20020307
 DT US 2001-873403 AI 20010604 (9)
 RLI Continuation-in-part of Ser. No. US 2000-625139, filed on 25 Jul 2000,
 PENDING
 PRAI US 2000-209266P 20000602 (60)
 DT Utility
 FS APPLICATION
 LN.CNT 4477
 INCL INCLM: 424/185.100
 INCLS: 424/190.100; 424/178.100; 530/391.100
 NCLM: 424/185.100
 NCL: 424/190.100; 424/178.100; 530/391.100
 IC [7]
 ICM: A61K039-40
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 L6 ANSWER 9 OF 19 USPATFILL
 AN 2002:297296 USPATFILL
 TI Methods for inhibition of membrane fusion-associated events, including
 respiratory syncytial virus transmission
 IN Bolognesi, Dani Paul, Durham, NC, United States
 Matthews, Thomas James, Durham, NC, United States
 Wild, Carl T., Durham, NC, United States
 Barney, Shawn O'Lin, Cary, NC, United States
 Lambert, Dennis Michael, Cary, NC, United States
 Letteway, Stephen Robert, Cary, NC, United States
 Langlois, Alphonse J., Durham, NC, United States
 Trimeris, Inc., Durham, NC, United States (U.S. corporation)
 PA US 6479055 BI 20021112
 PI US 1995-470896 19950606 (8)
 RLI Continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994,

now patented, Pat. No. US 6017536 Continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994 Continuation-in-part of Ser. No. US 1993-73028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933

DT Utility

PS GRANTED

LN CNT 26553

INCL INCLM: 424/211.100

NCL INCLM: 424/186.100; 530/324.000

NCLM: 424/211.100

NCLS: 424/186.100; 530/324.000

IC [7]

ICM: A61K039-145

EXF 435/5; 435/240.2; 424/184.1-189.1; 424/204.1-211.1; 424/225.1; 424/227.1; 424/230.1; 514/1; 514/2; 530/324; 530/350; 530/826

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 10 OF 19 CAPLUS

TI 2002:136555 USPATFOLL

Methods of modulating an immune response to antigen, and cells for use in the method

IN Segal, Andrew H., Boston, MA, United States

PA Whitehead Institute for Biomedical Research, Cambridge, MA, United States (U.S. corporation)

PI US 6403080 B1 20020611

AI US 1999-339523 19990624 (9)

RLI Division of Ser. No. US 1997-826259, filed on 27 Mar 1997, now patented, Pat. No. US 5951976 19960328 (60)

PRAI US 1996-14364P

DT Utility

FS GRANTED

LN CNT 2153

INCLM: 424/093.100

INCLS: 424/093.200; 424/093.210; 424/093.700; 424/093.710; 424/136.100; 435/325.000; 514/002.000; 514/012.000; 530/387.300

NCLM: 424/093.100

NCLS: 424/093.200; 424/093.210; 424/093.700; 424/093.710; 424/136.100; 435/325.000; 514/002.000; 514/012.000; 530/387.300

IC [7]

ICM: A01N063-00

EXF 1CS: A61K039-395; A61K038-00; C12P021-08

424/93.21; 424/93.7; 424/93.1; 424/93.2; 424/93.71; 424/136.1; 435/325; 514/12; 514/21; 530/387.3

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2003 ACS

AN 2002:899128 CAPLUS

DN 138:88135

TI Structure-function studies of the receptors for complement C1q

AU McGreal, E.; Gaege, P.

CS University of Oxford, Sir William Dunn School of Pathology, Oxford, OX1 3RE, UK

SO Biochemical Society Transactions (2002), 30(6), 1010-1014

COBEN: BCSTB5; ISSN: 0300-5127

PB Portland Press Ltd.

DT Journal: General Review

LA English

RE CNT 50

ALL CITATIONS AVAILABLE IN THE RE FORMAT

ALL CITED REFERENCES AVAILABLE FOR THIS RECORD

L6 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2003 ACS

AN 2001:866449 CAPLUS

DN 136:36328

TI Alpha 2 macroglobulin receptors as a heat shock protein receptor and uses thereof

IN Srivastava, Pramod K.

PA University of Connecticut Health Center, USA

SO PCT Int. Appl., 236 pp.

CODEN: PIXD2

DT Patent

LA English

FAN CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 2001092474 A1 20011206 WO 2001-US18041 20010604

W: AU, CA, JP

RM: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

PRAI US 2000-209095P P 20000602

US 2000-625137 A 20000725

US 2000-668724 A 20000922

US 2000-750972 A 20001228

RE CNT 1

ALL CITATIONS AVAILABLE IN THE RE FORMAT

ALL CITED REFERENCES AVAILABLE FOR THIS RECORD

L6 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2003 ACS

AN 2001:851435 CAPLUS

DN 136:1570

TI Compositions, kits, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases associated therewith

IN Hanahan, Catherine F.; Feldman, Marc; Trepcichio, William L.

PA Genetics Institute, Inc., USA; Kennedy Institute of Rheumatology

SO PCT Int. Appl., 115 pp.

CODEN: PIXD2

DT Patent

LA English

FAN CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 2001088199 A2 20011122 WO 2001-US16022 20010517

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, ME, MG, MK, MN, MW, MX, MY, NZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VA, YU, ZA, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM

RM: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GW, GN, HT, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, ME, MG, MK, MN, MW, MX, MY, NZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VA, YU, ZA, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GW, GN, HT, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, ME, MG, MK, MN, MW, MX, MY, NZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VA, YU, ZA, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM

PRAI US 2002039734 A1 20020404 US 2001-860655 20010517

US 2000-205204P P 20000518

L6 ANSWER 14 OF 19 CAPLUS

AN 2001:67794 USPATFOLL

TI Human respiratory syncytial virus peptides with antifusogenic and antiviral activities

IN Barney, Shawn O'Lin, Cary, NC, United States

PA Lambert, Dennis Michael, Cary, NC, United States

Peteway, Stephen Robert, Cary, NC, United States

Triimeris, Inc., Durham, NC, United States (U.S. corporation)

PI US 6228983 B1 20010508

US 1995-465264

US 1995-470896, filed on 6 Jun 1995

Continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994

Continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994

Continuation-in-part of Ser. No. US 1993-73028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933

DT Utility

FS GRANTED

LN CNT 32166

INCL: INCLM: 530/300.000
 INCLM: 530/324.000; 530/325.000; 530/326.000; 424/211.100; 424/186.100
 NCL: 530/300.000
 NCLM: 530/300.000
 NCLM: 424/186.100; 424/211.100; 530/324.000; 530/325.000; 530/326.000
 IC: 1CM: A61K038-00
 EXP: 530/350; 530/324-328; 530/300; 424/211.1
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2003 ACS
 AN 2000:908423 CAPLUS
 DN 134:203644
 TI Morphologic analysis correlates with gene expression changes in cultured
 F344 rat mesothelial cells
 AU Crosby, L. M.; Hyder, K. S.; DeAngelo, A. B.; Kepler, T. B.; Gaskill, B.;
 Benavides, G. R.; Yoon, L.; Morgan, K. T.; University of North Carolina at Chapel Hill, Curriculum in Toxicology/U.S.
 CS EPA NHEERL, Research Triangle Park, NC, 27711, USA
 SO Toxicology and Applied Pharmacology (2000), 169(3), 205-221
 CODEN: TAPAP9; ISSN: 0041-008X
 PB Academic Press
 DT Journal
 LA English
 RE CNT 60

ALL CITATIONS AVAILABLE IN THE RE FORMAT

THESE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD

L6 ANSWER 16 OF 19 MEDLINE
 AN 2001216038 MEDLINE
 DN 21205395 Pubmed ID: 11248808
 TI CD91: a receptor for heat shock protein
 9996.
 CM Comment in: Nat Immunol. 2000 Aug;1(2):100-1
 AU Binder R J; Han D K; Srivastava P K
 CS Center for Immunotherapy of Cancer and Infectious Diseases, University of
 NC Connecticut School of Medicine, Farmington, CT 06030, USA.
 CN C64394 (NCI)
 SO Nat Immunol. (2000 Aug) 1 (2) 151-5.
 CY United States
 DT Journal: Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 200105
 ED Entered STN: 20010521
 Laet Updated on STN: 20010521
 Entered Medline: 20010517

L6 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2003 ACS
 AN 1999:795994 CAPLUS
 DN 132:31744
 TI Gene probes used for genetic profiling in healthcare screening and
 planning
 AU Roberts Gareth Wyn
 PA Genosic Pharma Ltd., UK
 SO PCT Int. Appl., 745 pp.
 CODEN: PIXD2
 DT Patent
 LA English
 FAN CNT 2

PATENT NO. KIND DATE APPLICATION NO. DATE
 WO 9964627 A2 19991216 WO 1999-GB1780 19990604
 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,
 DE, DK, EE, ES, FI, GB, GD, GE, GH, GI, GR, GU, HU, ID, IL, IN, IS,

JP, KE, KG, KP, KR, KZ, LC, LK, LR, LU, LV, MD, MG, MK,
 MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
 TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ,
 MD, RU, TJ, TM
 RW, CH, CM, KE, LS, MW, SD, SL, SZ, UC, ZW, AT, BE, CH, CY, DE, DK,
 ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
 CI, CM, GN, GT, GW, ML, MR, NE, SN, TD, TG

PRAI GB 1998-12099 A 19980606
 GB 1998-13291 A 19980620
 GB 1998-13611 A 19980624
 GB 1998-13835 A 19980627
 GB 1998-14110 A 19980701
 GB 1998-14580 A 19980706
 GB 1998-15438 A 19980716
 GB 1998-15574 A 19980718
 GB 1998-15576 A 19980718
 GB 1998-16085 A 19980724
 GB 1998-16086 A 19980724
 GB 1998-16921 A 19980805
 GB 1998-17097 A 19980807
 GB 1998-17200 A 19980808
 GB 1998-17632 A 19980814
 GB 1998-17943 A 19980819

L6 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2003 ACS
 AN 1999:795993 CAPLUS
 DN 132:31743
 TI Gene probes used for genetic profiling in healthcare screening and
 planning
 AU Roberts Gareth Wyn
 PA Genosic Pharma Limited, UK
 SO PCT Int. Appl., 149 pp.
 CODEN: PIXD2
 DT Patent
 LA English
 FAN CNT 2

PATENT NO. KIND DATE APPLICATION NO. DATE
 WO 9964626 A2 19991216 WO 1999-GB1779 19990604
 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,
 DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
 JP, KE, KG, KP, KR, KZ, LC, LK, LR, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
 TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW, CH, CM, KE, LS, MW, SD, SL, SZ, UC, ZW, AT, BE, CH, CY, DE, DK,
 ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GN, GT, GW, ML, MR, NE, SN, TD, TG

PRAI GB 1998-12098 A 19980606
 GB 1998-28289 A 19981223
 GB 1998-16086 A 19980724
 GB 1998-16921 A 19980805
 GB 1998-17097 A 19980807
 GB 1998-17200 A 19980808
 GB 1998-17632 A 19980814
 GB 1998-17943 A 19980819
 WO 1999-GB1779 A 19990604

L6 ANSWER 19 OF 19 USPATFULTL
 AN 1999:141305 USPATFULTL
 TI Adjuvant for transcutaneous immunization
 IN Glenn, Gregory M., Bethesda, MD, United States
 PA Alving, Carl R., Bethesda, MD, United States
 PA The United States of America as represented by the U.S. Army Medical
 Research & Materiel Command, Washington, DC, United States (U.S.
 government)
 PI US 5980838 19991109
 AI US 1997-896085 19970717 (8)
 DT Continuation-in-part of Ser. No. US 1996-749164, filed on 14 Nov 1996
 FS Utility
 LN CNT 1988
 INCL INCLM: 424/184.100
 INCLS: 424/449.000; 424/450.000; 424/236.000; 424/240.100; 424/241.100;
 NCL NCLM: 424/184.100
 NCLS: 424/085.100; 424/240.100; 424/241.100; 424/275.100; 424/449.000;
 IC [6]
 ICM: A61K039-00
 ICS: C07K014-005; C07K014-195
 EXF 424/449; 424/450; 424/184.1; 424/236; 424/240.1; 424/241.1; 424/275.1;
 530/363; 530/403
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> s agonist? and 11
 L7 1585 AGONIST? AND L1

=> s 17 and 12
 L8 4 L7 AND L2

=> d 1-4

L8 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2003 ACS
 AN 2001.886449 CAPLUS
 DN 136:36328
 TI Alpha 2 macroglobulin receptors as
 a heat shock protein receptor and uses
 thereof
 IN Srivastava, Pramod K.
 PA University of Connecticut Health Center, USA
 SO PCT Int. Appl., 236 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN CNT 1
 PATENT NO. KIND DATE APPLICATION NO. DATE
 PI WO 2001092474 A1 20011206 WO 2001-US18041 20010604
 W: AU, CA, JP
 R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
 PT, SE, TR
 PRAI US 2000-209095P P 20000602
 US 2000-625137 A 20000725
 US 2000-668724 A 20000932
 US 2000-750972 A 20001228
 RE CNT 1
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS
 AN 2001.319729 CAPLUS
 DN 134:320865

TI Regulation of apob for diagnosis, treatment and drug screening for
 cardiovascular and metabolic disorders or syndromes
 IN Fisher, Edward A.; Williams, Kevin Jon
 PA Thomas Jefferson University, USA
 SO PCT Int. Appl., 59 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN CNT 1
 PATENT NO. KIND DATE APPLICATION NO. DATE
 PI WO 2001030354 A1 20010503 WO 2000-US29699 20001026
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
 CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GR, GU, HK, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
 LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NZ, NI, NO, NZ, PL, PT, RO, RU,
 SD, SE, SG, SI, SK, SL, ST, SV, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
 YU, ZA, ZW, AM, AZ, BY, BG, BR, BY, KG, KZ, MD, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
 CF, CG, CI, CM, CA, GN, GW, ML, MR, NE, SN, TD, TG
 PRAI US 1999-161537P P 19991026
 RE CNT 1
 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 4 USPATFULTL
 AN 2002.315069 USPATFULTL
 TI Compositions and methods for treatment of neoplastic disease
 IN Terman, David S., Pebble Beach, CA, UNITED STATES
 PI US 2002177551 A1 20021128
 AI US 2001-870759 A1 20010530 (9)
 PRAI US 2000-208128P 20000531 (60)
 DT Utility
 FS APPLICATION
 LN CNT 17323
 INCL INCLM: 514/012.000
 INCLS: 435/325.000; 530/350.000
 NCL NCLM: 514/012.000
 NCLS: 435/325.000; 530/350.000
 IC [7]
 ICM: A61K038-17
 ICS: C12N005-06; C07K014-705
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 4 OF 4 USPATFULTL
 AN 2002.259381 USPATFULTL
 TI Materials and methods relating to lipid metabolism
 IN Ballinger, Dennis G., Menlo Park, CA, UNITED STATES
 LOeb, Deborah, San Jose, CA, UNITED STATES
 Montgomery, Julie R., Santa Cruz, CA, UNITED STATES
 Tang, Y. Tom, San Jose, CA, UNITED STATES
 Zhou, Ping, Cupertino, CA, UNITED STATES
 Goodrich, Ryle, San Jose, CA, UNITED STATES
 Liu, Chenghua, San Jose, CA, UNITED STATES
 Asundi, Vinod, Foster City, CA, UNITED STATES
 Zhao, Qing A., San Jose, CA, UNITED STATES
 Weinman, Tom, Stanford, CA, UNITED STATES
 Dmanac, Radoje T., Palo Alto, CA, UNITED STATES
 Ren, Feiyang, Cupertino, CA, UNITED STATES
 Qian, Xiaohong B., San Jose, CA, UNITED STATES
 Wang, Dunrui, Poway, CA, UNITED STATES
 PI US 2002142953 A1 20021003
 US 2001-835996 A1 20010416 (9)
 CONTINUATION-IN-PART OF Ser. No. US 2000-714936, filed on 17 Nov 2000,
 PENDING CONTINUATION-IN-PART OF Ser. No. US 2000-667298, filed on 22 Sep

2000, PENDING Continuation-in-part of Ser. No. US 2000-631451, filed on 3 Aug 2000, PENDING Continuation-in-part of Ser. No. US 2000-598042, filed on 20 Jun 2000, PENDING

PRAI US 2000-197137P 20000414 (60)

DT Utility

FS APPLICATION

LN.CNT 9120

INCL INCLM: 514/012.000

NCL INCLM: 514/012.000

IC [7]

ICS: C07H021-04; C12N009-16; C12P021-02; C12N005-06; C07K014-775

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d his

FILE 'HOME' ENTERED AT 15:25:49 ON 20 FEB 2003

ENTERED AT 15:26:27 ON 20 FEB 2003

FILE 'MEDLINE, CANCERLIT, BIOSIS, CONFSCI, EMBASE, CAPLUS, USPATFULL'

72563 S HEAT (A) SHOCK (A) PROTEIN

40 S L1 AND ALPHA (A) 2 (A) MACROGLOBULIN (A) RECEPTOR

12721 S L1 AND ANTIBODY

21 S L4 AND L2

19 DUP REM L5 (2 DUPLICATES REMOVED)

1585 S AGONIST? AND L1

4 S L7 AND L2

=> s 11 and peptide?

8637 L1 AND PEPTIDE?

=> s 19 and 12

27 L9 AND L2

=> dup rem 110

PROCESSING COMPLETED FOR L10

24 DUP REM L10 (3 DUPLICATES REMOVED)

=> s 111 and modulates?

11 L11 AND MODULATE?

=> d 1-11

L12 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2003 ACS

AN 2001:886449 CAPLUS

DN 136:36328

TI Alpha 2 macroglobulin receptors as

a heat shock protein receptor and uses

thereof

IN Srivastava, Pramod K.

PA University of Connecticut Health Center, USA

SO PCT Int. Appl., 236 PP.

COEN: PIXXD2

DT Patent

LA English

PAN.CNT 1

PATENT NO.

KIND DATE

MO 2001092474 A1 20011206

APPLICATION NO.

DATE

MO 2001-US18041 20010604

W: AU, CA, JP
RM: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, TR

PRAI US 2000-209095P P 20000602

US 2000-625137 A 20000725

US 2000-668724 A 20000922

US 2000-750972 A 20001228

RE.CNT 1

THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 11 USPATFULL

AN 2003:40533 USPATFULL

TI Methods for the inhibition of Epstein-Barr virus transmission employing

anti-viral peptides capable of abrogating viral fusion and transmission

IN Barney, Shawn O'Lin, Cary, NC, United States

Lamberg, Dennis Michael, Cary, NC, United States

Peteway, Stephen Robert, Cary, NC, United States

Trimeris, Inc., Durham, NC, United States (U.S. corporation)

PI US 6518013 B1 20030211

AI US 1995-485546 19950607 (8)

Continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994,

now patented, Pat. No. US 6017536 Continuation-in-part of Ser. No. US

1994-255208, filed on 7 Jun 1994 Continuation-in-part of Ser. No. US

1993-73028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933

Utility

GRANTED

LN.CNT 24700

INCL INCLM: 435/005.000

INCLM: 424/230.100; 530/300.000; 530/324.000; 530/325.000; 530/326.000

NCL INCLM: 435/005.000

NCLM: 424/230.100; 530/300.000; 530/324.000; 530/325.000; 530/326.000

IC [7]

ICM: C12N001-70

EXF 435/5; 530/300; 530/324-329; 530/350; 424/230.1

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 3 OF 11 USPATFULL

AN 2002:315069 USPATFULL

TI Compositions and methods for treatment of neoplastic disease

IN Terman, David S., Pebble Beach, CA, UNITED STATES

PI US 2002177551 A1 20021128

AI US 2001-870759 A1 20010530 (9)

PRAI US 2000-208128P 20000531 (60)

Utility

APPLICATION

LN.CNT 17323

INCL INCLM: 514/012.000

INCLM: 435/325.000; 530/350.000

NCL INCLM: 514/012.000

NCLM: 435/325.000; 530/350.000

IC [7]

ICM: A61K038-17

ICS: C12N005-06; C07K014-705

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 4 OF 11 USPATFULL

AN 2002:297296 USPATFULL

TI Methods for inhibition of membrane fusion-associated events, including

respiratory syncytial virus transmission

Bolognesi, Dani Paul, Durham, NC, United States

Mathews, Thomas James, Durham, NC, United States

Wild, Carl T., Durham, NC, United States

Barney, Shawn O'Lin, Cary, NC, United States

Lamberg, Dennis Michael, Cary, NC, United States

Peteway, Stephen Robert, Cary, NC, United States

PA Langlois, Alphonse J., Durham, NC, United States
 PI Trimeris, Inc., Durham, NC, United States (U.S. corporation)
 AI US 6479055 B1 20021112
 IN US 1995-470896 19950606 (8)
 RLI Continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994,
 now patented, Pat. No. US 6017536 Continuation-in-part of Ser. No. US
 1994-235208, filed on 7 Jun 1994 Continuation-in-part of Ser. No. US
 1993-73028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933

DT Utility
 FS GRANTED
 LN.CNT 26553
 INCL INCLM: 424/211.100
 INCLS: 424/186.100; 530/324.000
 NCLM: 424/211.100
 NCLS: 424/186.100; 530/324.000

IC [7]
 ICM: A61K039-145
 EXF 435/5; 435/240.2; 424/184.1-189.1; 424/204.1-211.1; 424/225.1;
 424/227.1; 424/230.1; 514/1; 514/2; 530/324; 530/350; 530/826

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 5 OF 11 USPTAFUL
 TI 2002:259381 USPTAFUL
 IN Materials and methods relating to lipid metabolism
 Ballinger, Dennis G., Menlo Park, CA, UNITED STATES
 Loeb, Deborah, San Jose, CA, UNITED STATES
 Montgomery, Julie R., Santa Cruz, CA, UNITED STATES
 Tang, Y. Tom, San Jose, CA, UNITED STATES
 Zhou, Ping, Cupertino, CA, UNITED STATES
 Goodrich, Ryle, San Jose, CA, UNITED STATES
 Liu, Chenghua, San Jose, CA, UNITED STATES
 Asundi, Vinod, Foster City, CA, UNITED STATES
 Zhao, Qing A., San Jose, CA, UNITED STATES
 Wehrman, Tom, Stanford, CA, UNITED STATES
 Drmanac, Radoje T., Palo Alto, CA, UNITED STATES
 Ren, Feiyun, Cupertino, CA, UNITED STATES
 Qian, Xiaohong B., San Jose, CA, UNITED STATES
 Wang, Dunhui, Poway, CA, UNITED STATES
 PI US 2002142953 AI 20021003
 AI US 2001-835996 AI 20010416 (9)
 RLI Continuation-in-part of Ser. No. US 2000-714936, filed on 17 Nov 2000,
 PENDING Continuation-in-part of Ser. No. US 2000-667298, filed on 22 Sep
 2000, PENDING Continuation-in-part of Ser. No. US 2000-631451, filed on
 3 Aug 2000, PENDING Continuation-in-part of Ser. No. US 2000-598042,
 filed on 20 Jun 2000, PENDING

PRAI US 2000-197137P 20000414 (60)
 DT Utility
 FS APPLICATION
 LN.CNT 9120
 INCL INCLM: 514/012.000
 INCLS: 435/069.100; 435/325.000; 435/320.100; 530/359.000; 435/196.000;
 536/023.200
 NCLM: 514/012.000
 NCLS: 435/069.100; 435/325.000; 435/320.100; 530/359.000; 435/196.000;
 536/023.200

IC [7]
 ICM: A61K038-17
 EXF ICS: C07H021-04; C12N009-16; C12P021-02; C12N005-06; C07K014-775

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 6 OF 11 USPTAFUL
 TI 2002:206116 USPTAFUL
 IN Toxicant-induced differential gene expression
 Reichardt-Olson, John F., Montclair, NJ, UNITED STATES
 PI US 2002110808 AI 20020815

AI US 2000-489220 AI 20000121 (9)
 DT Utility
 FS APPLICATION
 LN.CNT 5161
 INCL INCLM: 435/006.000
 INCLS: 435/091.200; 536/023.100
 NCLM: 435/006.000
 NCLS: 435/091.200; 536/023.100

IC [7]
 ICM: C12Q001-68
 EXF ICS: C07H021-02; C07H021-04; C12P019-34

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 7 OF 11 USPTAFUL
 TI 2002:164658 USPTAFUL
 IN Immunotherapeutic methods for extracorporeal modulation of CD36 and its
 ligands
 PI Srivastava, Pramod K., Avon, CT, UNITED STATES
 AI US 2002086276 AI 20020704
 AI US 2000-750973 AI 20001228 (9)
 DT Utility
 FS APPLICATION
 LN.CNT 1813
 INCL INCLM: 435/002.000
 INCLS: 424/140.100
 NCLM: 435/002.000
 NCLS: 424/140.100

IC [7]
 ICM: A61K039-395

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 8 OF 11 USPTAFUL
 TI 2002:136555 USPTAFUL
 IN Methods of modulating an immune response to antigen, and cells for use
 in the method
 PI Segal, Andrew H., Boston, MA, United States
 AI Whitehead Institute for Biomedical Research, Cambridge, MA, United
 States (U.S. corporation)
 PI US 6403080 B1 20020611
 AI US 1999-339523 19990624 (9)
 RLI Division of Ser. No. US 1997-826259, filed on 27 Mar 1997, now patented,
 Pat. No. US 5951976
 PRAI US 1996-14364P 19960328 (60)
 DT Utility
 FS GRANTED
 LN.CNT 2153
 INCL INCLM: 424/093.100
 INCLS: 424/093.200; 424/093.210; 424/093.700; 424/093.710; 424/136.100;
 435/325.000; 514/002.000; 514/012.000; 530/387.300
 NCLM: 424/093.100
 NCLS: 424/093.200; 424/093.210; 424/093.700; 424/093.710; 424/136.100;
 435/325.000; 514/002.000; 514/012.000; 530/387.300

IC [7]
 ICM: A01N063-00
 EXF ICS: A61K039-395; A61K038-00; C12B021-08
 424/93.21; 424/93.7; 424/93.1; 424/93.2; 424/93.71; 424/136.1; 435/325;
 514/12; 514/21; 530/387.3

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 9 OF 11 USPTAFUL
 TI 2002:66639 USPTAFUL
 IN Compositions comprising heat shock proteins
 or alpha(2) macroglobulin, antigenic molecules and saponins, and methods
 of use thereof
 PI Armen, Gato H., Manhasset, NY, UNITED STATES

PI US 2002037290 A1 20020328
 AI US 2001-909778 A1 20010720 (9)
 PRAI US 2000-223133P 20000807 (60)
 DT Utility
 FS APPLICATION
 LN CNT 4136
 INCL INCLM: 424/178.100
 INCLS: 514/012.000; 514/026.000
 NCL NCLM: 424/178.100
 NCLS: 514/012.000; 514/026.000
 IC (7)
 ICM: A61K039-395
 ICS: A61K038-17
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 10 OF 11 USPATFULT
 AN 2001:67794 USPATFULT
 TI Human respiratory syncytial virus peptides with antitumorigenic and
 antiviral activities
 IN Barney, Shawn O'Lin, Cary, NC, United States
 Lambert, Dennis Michael, Cary, NC, United States
 Petteaway, Stephen Robert, Cary, NC, United States
 Trimeris, Inc., Durham, NC, United States (U.S. corporation)
 PA US 1995-485264 B1 20010508
 PI US 6228983
 AI US 1995-485264 19950607 (8)
 RLI Division of Ser. No. US 1995-470896, filed on 6 Jun 1995
 Continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994
 Continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994
 Continuation-in-part of Ser. No. US 1993-73028, filed on 7 Jun 1993, now
 patented, Pat. No. US 5464933

DT Utility
 FS Granted
 LN CNT 32166
 INCL INCLM: 530/300.000
 INCLS: 530/324.000; 530/325.000; 530/326.000; 424/211.100; 424/186.100
 NCL NCLM: 530/300.000
 NCLS: 424/186.100; 424/211.100; 530/324.000; 530/325.000; 530/326.000
 IC (7)
 ICM: A61K038-00
 ICS: 530/350; 530/324-329; 530/300; 424/211.1
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 11 OF 11 USPATFULT
 AN 1999:141305 USPATFULT
 TI Adjuvant for transcutaneous immunization
 IN Glenn, Gregory M., Bethesda, MD, United States
 Alving, Carl R., Bethesda, MD, United States
 PA The United States of America as represented by the U.S. Army Medical
 Research & Materiel Command, Washington, DC, United States (U.S.
 government)
 PI US 5980898 19991109
 AI US 1997-896085 19970717 (8)
 RLI Continuation-in-part of Ser. No. US 1996-749164, filed on 14 Nov 1996
 DT Utility
 FS Granted
 LN CNT 1988
 INCL INCLM: 424/184.100
 INCLS: 424/449.000; 424/450.000; 424/236.000; 424/240.100; 424/241.100;
 424/275.100; 530/363.000; 530/403.000
 NCL NCLM: 424/184.100
 NCLS: 424/085.100; 424/240.100; 424/241.100; 424/275.100; 424/449.000;
 424/450.000; 530/363.000; 530/403.000
 IC (6)
 ICM: A61K039-00
 ICS: C07K014-005; C07K014-195

EXF 424/449; 424/450; 424/184.1; 424/236; 424/240.1; 424/241.1; 424/275.1;
 530/363; 530/403
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d kwic 11

L12 ANSWER 11 OF 11 USPATFULT
 SUMM "Large molecules normally do not get across the intact
 mammalian skin. It is thus impossible to immunize epicutaneously with
 simple peptide or protein solutions." They concluded, "The
 dermally applied liposomal or mixed micellar immunogens are biologically
 as inactive as simple protein."
 DETD Antigen obtained through recombinant means or peptide
 synthesis, as well as antigen of the invention obtained from natural
 sources or extracts, may be purified by means of:
 DETD . . . granulocyte-monocyte-colony stimulating factor) (reviewed in
 Nobria and Rubin, 1994), a muramyl dipeptide derivative (e.g.,
 murabutide, threonyl-MDP or muramyl tripeptide), a heat
 shock protein or a derivative, a derivative of
 Leishmania major leif (Skelley et al., 1995), cholera toxin or cholera
 toxin B, a . . .
 DETD Optionally, an activator of langerhans cells may be used as an adjuvant.
 Examples of such activators include: inducers of heat
 shock protein; contact sensitizers (e.g.,
 trinitrochlorobenzene, dinitrofluorobenzene, nitrogen mustard,
 pentadecylcatechol); toxins (e.g., Shiga toxin, Staph enterotoxin B);
 lipopolyaccharides, lipid A, or derivatives.
 DETD . . . immune response to cholera toxin (CT) in rabbits and to a
 synthetic protein consisting of a malaria oligopeptide containing four
 tetra-peptides (Asn-Ala-Asn-Pro) conjugated to BSA. The
 authors found that the immune response to cholera toxin or to the
 synthetic malaria protein. . .
 DETD . . . the groups could be detected. ETA differs from CT and LT in
 that ETA is a single 613 amino acid peptide with A and B
 domains on the same peptide and binds to an entirely different
 receptor, the .alpha.2-macroglobulin
 receptor/low density lipoprotein receptor-related protein
 (Kounnas et al., 1992). Despite the dissimilarities between ETA and CT
 in size, structure, and binding. . .
 DETD Bodanszky, M. (1993) Peptide Chemistry, Springer-Verlag, New
 York.
 DETD . . . L. F., et al. (1992b) Safety, immunogenicity, and efficacy of a
 Plasmodium falciparum vaccine comprising a circumsporozoite protein
 repeat region peptide conjugated to Pseudomonas aeruginosa
 toxin A. Infect. Immun., 60:1834-1839.
 DETD Pessi, A., et al. (1991) Lack of H-2 restriction of the Plasmodium
 falciparum (NANP) sequence as multiple antigen peptide. Eur.
 J. Immunol., 24:2273-2276.
 DETD Porcador, A., et al. (1997) Intranasal immunization with CTL epitope
 peptides from HIV-1 or ovalbumin and the mucosal adjuvant
 cholera toxin induces peptide-specific CTLs and protection
 against tumor development in vivo. J. Immunol., 158:834-841.
 DETD Schwarzenberger, K., and Udey, M. C. (1996) Contact allergens and
 epidermal proinflammatory cytokines modulate langerhans cell
 E-cadherin expression in situ. J. Invest. Dermatol., 106:553-558.
 DETD Tam, J. P. (1988) Synthetic peptide vaccine design: Synthesis
 and properties of a high-density multiple antigenic peptide
 system. Proc. Natl. Acad. Sci. U.S.A., 85:5409-5413.
 DETD T-cell receptor peptides: Results of a double-blind pilot
 trial. Nature Medicine, 2:1109-1115.
 DETD Wang, R., et al. (1995) Induction of protective polyclonal antibodies by
 immunization with a Plasmodium yoelii circumsporozoite protein multiple
 antigen peptide vaccine. J. Immunol., 154:2784-2793.

- DETD Wisdom, G. B. (1994) *Peptide Antigens*, IRL Press, Oxford.
- => d kwic 9
- L12 ANSWER 9 OF 11 USPATFULL
TI Compositions comprising heat shock proteins
or alpha(2) macroglobulin, antigenic molecules and saponins, and methods
of use thereof
AB . . . diseases, and primary and metastatic neoplastic diseases. In
the practice of the invention, the compositions are employed comprising:
(a) a heat shock protein (hsp) or an
alpha(2) macroglobulin (.alpha.2M); (b) a saponin; and, optionally, (c)
an antigenic molecule. The antigenic molecule displays the antigenicity.
- SUMM . . . diseases (i.e., cancer), neurodegenerative or amyloid diseases,
and autoimmune diseases, and methods of formulating the compositions.
The compositions comprise a heat shock
protein (hsp) or alpha(2) macroglobulin (.alpha.2M) and a saponin
when used for the treatment and prevention of an autoimmune disease. The
compositions.
SUNM . . . Biology of the Cell, p. 1228). Both cytotoxic T cells and
helper T cells recognize antigen in the form of peptide
fragments that are generated by the degradation of foreign protein
antigens inside the target cell, and both, therefore, depend on major
histocompatibility complex (MHC) molecules, which bind these
peptide fragments, carry them to the cell surface, and present
them there to the T cells (Alberts et al., 1d.). MHC.
SUNM . . . homology between them, and showed that gp96 and p84/86 were,
respectively, the endoplasmic reticular and cytosolic counterparts of
the same heat shock proteins (Srivastava
et al., 1988, Immunogenetics 28:205-207; Srivastava et al., 1991, Curr.
Top. Microbiol. Immunol. 167:109-123). Further, hsp70 was shown to .
elicit immunity to the tumor from which it was isolated but not to
antigenically distinct tumors. However, hsp70 depleted of
peptides was found to lose its immunogenic activity (Udono and
Srivastava, 1993, J. Exp. Med. 178:1351-1356). These observations
suggested that the heat shock proteins are
not immunogenic per se, but instead form noncovalent complexes with
antigenic peptides, and the complexes elicit specific immunity
to the antigenic peptides (Srivastava, 1993, Adv. Cancer Res.
62:153-177; Udono et al., 1994, J. Immunol., 152:5398-5403; Suto et al.,
1995, Science, 269:1585-1588).
- SUNM [0012] Noncovalent complexes of hsps and peptide, purified
from cancer cells, can be used for the treatment and prevention of
cancer and have been described in PCT . . . 17, 1998, respectively,
each of which is incorporated by reference herein in its entirety. The
isolation and purification of stress protein-peptide complexes
has been described, for example, from pathogen-infected cells, and can
be used for the treatment and prevention of infection.
intracellular pathogens, including bacteria, protozoa, fungi and
parasites (see e.g., PCT Publication WO 95/24923, dated Sep. 21, 1995).
Immunogenic stress protein-peptide complexes can also be
prepared by in vitro complexing of stress protein and antigenic
peptides, and the uses of such complexes for the treatment and
prevention of cancer and infectious diseases has been described in .
publication WO 97/10000, dated Mar. 20, 1997 and U.S. Pat. No.
6,030,618 issued Feb. 29, 2000. The use of stress protein-
peptide complexes for sensitizing antigen presenting cells in
vitro for use in adoptive immunotherapy is described in PCT publication
WO 97/10002.
- SUNM [0013] 2.3. Heat Shock Proteins and Their
Roles in Antigen Presentation
SUNM [0014] 2.3.1. Heat Shock Proteins
SUNM [0015] Heat shock proteins (hsps), also
- SUNM referred to as stress proteins, were first identified as proteins
synthesized by cells in response to heat shock. . . .
[0016] Heat shock proteins are among the
most highly conserved proteins in existence. For example, Dnak, the
hsp70 from E. coli, has about 50% . . .
SUNM . . . proteins in normal cells (Lindquist et al., 1988, Ann. Rev.
Genetics 22:631-677). The hsps are capable of binding proteins or
peptides, and of releasing the bound proteins or
peptides in the presence of adenosine triphosphate (ATP) or low
pH.
SUNM . . . present antigens on the cell surface of antigen-presenting
cells. Cytotoxic T lymphocytes (CTLs) then recognize MHC molecules and
their associated peptides and kill the target cell. Antigens
are processed by two distinct antigen processing routes depending upon
whether their origin is . . .
SUNM [0020] The heat shock protein gp96
chaperones a wide array of peptides, depending upon the source
from which gp96 is isolated (for review, see Srivastava et al., 1998,
Immunology 8: 657-665). Tumor-derived gp96 carries tumor-antigenic
peptides (Ishii et al., 1999, J. Immunology 162:1303-1309), gp96
preparations from virus-infected cells carry viral epitopes (Suto and
Srivastava, 1995, Science. . . (Arnold et al., 1995, J. Exp.
Med. 182:885-889; Breloer et al., 1998, Eur. J. Immunol. 28:1016-1021).
The association of gp96 with peptides occurs in vivo (Menoret
and Srivastava, 1999, Biochem. Biophys. Research Commun. 262:813-818).
gp96-peptide complexes, whether isolated from cells (Blachere et
al., 1997, Science 278:117-120), or reconstituted in vitro (Blachere et
al., 1997, J. . . 186:1183-1406) are excellent immunogens and have
been used extensively to elicit CD8+ T cell responses specific for the
gp96-chaperoned antigenic peptides.
SUNM [0021] The capacity of gp96-peptide complexes to elicit an
immune response is dependent upon the transfer of the peptide
to MHC class I molecules of antigen-presenting cells (Suto and
Srivastava, 1995, supra). Endogenously synthesized antigens chaperoned
by gp96 in CD8+ T cells requires macrophages. However, the process
whereby exogenously-introduced gp96-peptide complexes elicit
the antigen-specific CD8+ T cell response is not completely understood
since there is no established pathway for the translocation of
extracellular antigens into the class I presentation machinery. Yet
antigenic peptides of extracellular origin associated with
hsps are somehow salvaged by macrophages, channeled into the endogenous
pathway, and presented by MHC.
SUNM [0022] Several models have been proposed to explain the delivery of
extracellular peptides for antigen presentation. One proposal,
known as the "direct transfer" model, suggests that hsp-chaperoned
peptides are transferred to MHC I molecules on the cell surface
of macrophages for presentation to CD8+ T lymphocytes. Another
suggestion, . . . al., 1994, Immunogenetics 39:93-98). Others have
suggested that a novel intracellular trafficking pathway may be involved
for the transport of peptides from the extracellular medium
into the lumen of the ER (Day et al., 1997, Proc. Natl. Acad. Sci.
94:8064-8069; Nicchitta, . . . the cytosol where it would enter the
normal class I pathway; and/or (b) digest ingested material in lysosomes
and reexport peptides for loading on the surface to class I
molecules (Bevan, 1995, J. Exp. Med. 182:639-41).
[0023] Still others have proposed a receptor-mediated pathway for the
delivery of extracellular peptides to the cell surface of APCs
for antigen presentation. In view of the extremely small quantity of
gp96-chaperoned antigenic peptides required for immunization
(Blachere et al., 1997, supra), and the strict dependence of
immunogenicity of gp96-peptide complexes on functional antigen
presenting cells (APCs) (Udono et al., 1994, Proc. Natl. Acad. Sci.
U.S.A. 91:3077-3081), APCs had been . . . receptor is thought to be
used in the uptake of gp96 (Clupitru et al., 1998, J. Exp. Med.,

187:685-691). The $\alpha(2)$ macroglobulin receptor, also known as CD91, has proven to be a more universal receptor for hsp96, with binding to gp96, hsp90, hsp70, and surfaces of other cells, the APCs. APCs can trap lymph- and blood-borne antigens and after internalization and degradation, present antigenic peptide fragments, bound to cell-surface molecules of the major histocompatibility complex (MHC), to T cells. APCs may then activate T cells.

[0030] $\alpha(2)$ macroglobulin promiscuously binds to proteins and peptides with nucleophilic amino acid side chains in a covalent manner (Chu et al., 1994, *Ann. N.Y. Acad. Sci.* 737:291-307) and, in its entirety, α -2M directly competes for the binding of heat shock protein gp96 to the α -2M, indicating that α -2M and hsp96 may bind to a common recognition site on the α -2M (Binder et al., 2000, *Nature Immunology* 1(2), 151-154). Additionally, α -2M-antigenic peptide complexes prepared in vitro can be administered to animals to generate a cytotoxic T cell response specific to the antigenic. Immunol. 166:4968-72). Thus, because hsp96 and α -2M have a number of common functional attributes, such as the ability to bind peptide, the recognition and uptake by the α -2M, and the stimulation of a cytotoxic T cell response, α -2M can be used.

(White et al., 1991, "A purified saponin acts as an adjuvant for a T-independent antigen," in: *Immunobiology of Proteins and Peptides*, Vol. VI (Krause ed.), Plenum Press, New York, pp. 207-210). The immunogenicity of the vaccine was further increased by conjugating.

[0044] The ability of adjuvants to modulate the isotype distribution and IgG subclass distribution of antibody response to an antigen through the promotion of Ig subclass switching.

substantially lack antigenic molecules, are particularly useful in treating an autoimmune disorder. "Antigenic molecule" as used herein refers to a peptide or other molecule with which hsp96 are endogenously associated in vivo (e.g., in precancerous or cancerous tissue), as well as hsp96 are not complexed in vivo) or antigenic/immunogenic fragments and derivatives thereof. Such exogenous antigens and fragments and derivatives (both peptide and non-peptide) thereof for use in complexing with hsp96 or α -2M, can be selected from among those known in the art, as cancer cell, a cell infected with an infectious organism or a cell or structure, e.g., extracellular deposits or plaques comprising peptide and/or protein fibrils, that displays the hallmarks of a neurodegenerative or amyloid disease. In certain embodiments, the outcome of eliciting

the saponin, and the antigenic molecule are combined simultaneously. In another embodiment, purified hsp96 or α -2M is stripped of bound peptide and antigenic molecule, or antigenic molecule previously covalently linked to saponin, is bound to said hsp96 or α -2M in vitro.

[0067] In accordance with the methods described herein, immunogenic or antigenic peptides that are endogenously complexed to hsp96 or α -2M can be used as specific antigenic molecules. For example, such peptides may be prepared that stimulate cytotoxic T cell responses against different tumor antigens (e.g., tyrosinase, gp100, melan-A, gp75, mucins, etc.), or a fragment thereof, or a prion protein, and their antigenic derivatives. In the embodiment wherein the antigenic molecules are peptides noncovalently complexed to hsp96 or α -2M in vivo, the complexes can be isolated from cells, or alternatively, produced in vitro.

use specific antigenic molecules by complexing to hsp96 in vitro, hsp96 can be purified for such use from the endogenous hsp-peptide complexes in the presence of ATP or low pH (or chemically synthesized or recombinantly produced). The protocols described herein may be used to isolate hsp-peptide complexes.

or the hsp96 alone, from any eukaryotic cells for example, tissues, isolated cells, or immortalized eukaryotic cell lines infected.

using recombinant methods known in the art (see Szure et al., 1997, *Proc. Natl. Acad. Sci. U.S.A.* 94: 1146-51). α -2M-antigenic peptide fusions are then expressed and isolated. By specifically designing the antigenic peptide portion of the molecule, such fusion proteins can be used to elicit an immune response and in immunotherapy against target.

of the above embodiments, the first and/or second antigen, when present in the composition, is a synthetic or recombinantly generated peptide.

cell, can be used in the present methods for producing α -2M polypeptide-antigenic molecule complexes. The cancer cells provide the antigenic peptides which become associated covalently or noncovalently with the expressed α -2M polypeptide. α -2M polypeptide-antigenic molecule complexes are then purified from the.

vitro. Immunogenic α -2M polypeptide-antigenic molecule complexes can be generated in vitro by coupling of an α -2M polypeptide with an antigenic peptide. Procedures for forming such α -2M-antigenic molecule complexes and methods for isolating antigenic peptides are described below.

the nucleophilic activation, employing heat (Gr-o slashed.n and Pizzo, 1998, *Biochemistry*, 37: 6009-6014). Such conditions that allow fortuitous trapping of peptides by α -2M are employed to prepare the α -2M-antigenic complexes for use in the invention. Methods for such covalent coupling.

2 hrs at 25 degree C. The preparations can be centrifuged through a Centricon 10 assembly (Millipore) to remove any unbound peptide. Alternatively, free antigenic molecule may be removed by passage over a gel permeation column. The association of the peptides with the α -2M polypeptide can be assayed by SDS-PAGE. This is the preferred method for in vitro complexing of antigenic molecules isolated from MHC-antigenic molecule complexes, or peptides dissociated from endogenous α -2M-antigenic molecule complexes.

[0111] 4.2.2. Preparation and Purification of hsp70-peptide Complexes

[0112] The purification of hsp70-peptide complexes has been described previously, see, for example, Udono et al., 1993, *J. Exp. Med.* 178:1391-1396. A procedure that may.

[0115] Fractions strongly immunoreactive with the anti-hsp70 antibody are pooled and the hsp70-peptide complexes precipitated with ammonium sulfate: specifically with a 50%-70% ammonium sulfate cut. The resulting precipitate is then harvested by centrifugation.

[0116] The hsp70-peptide complex can be purified to apparent homogeneity using this method. Typically 1 mg of hsp70-peptide complex can be purified from 1 g of cells/tissue.

[0117] An improved method for purification of hsp70-peptide complexes comprises contacting cellular proteins with ADP or a nonhydrolyzable analog of ATP affixed to a solid substrate, such that.

ADP affixed to a solid substrate (e.g., ADP-agarose). The resulting hsp70 preparations are higher in purity and devoid of contaminating peptides. The hsp70 yields are also increased significantly by about more than 10 fold. Alternatively, chromatography with nonhydrolyzable analogs of ATP, instead of ADP, can be used for purification of hsp70-peptide complexes. By way of example but not limitation, purification of hsp70-peptide complexes by ADP-agarose chromatography can be carried out as follows:

ADP-agarose column. The column is washed in buffer and is eluted with 5 column volumes of 3 mM ADP. The hsp70-peptide complexes elute in fractions 2 through 10 of the total 15 fractions which elute. The eluted fractions are analyzed by SDS-PAGE. The hsp70-peptide complexes can be purified to apparent homogeneity using this procedure.

- SUMM [0119] 4.2.3. Preparation and Purification of hsp90-peptide complexes
[0123] The eluted fractions are fractionated by SDS-PAGE and fractions containing the hsp90-peptide complexes identified by Western immunoblotting using an anti-hsp90 antibody such as 3G3 (Affinity Bioreagents). hsp90-peptide complexes can be purified to apparent homogeneity using this procedure. Typically, 150-200 μ g of hsp90-peptide complex can be purified from 1 g of cells/tissue.
- SUMM [0124] 4.2.4. Preparation and Purification of gp96-peptide complexes
[0125] nuclei and other debris. The supernatant from this centrifugation step is then recentrifuged at 100,000 g for 90 minutes. The gp96-peptide complex can be purified either from the 100,000 pellet or from the supernatant.
- SUMM [0126] procedure, however, may be modified by two additional steps, used either alone or in combination, to consistently produce apparently homogeneous gp96-peptide complexes. One optional step involves an ammonium sulfate precipitation prior to the Con A purification step and the other optional:
[0127] concentrations of 2 mM, respectively. Then the sample is purified by either the unmodified or the modified method for isolating gp96-peptide complex from the 100,000 g supernatant, see above.
- SUMM [0134] The gp96-peptide complexes can be purified to apparent homogeneity using this procedure. About 10-20 μ g of gp96 can be isolated from 1 μ g of cells.
- SUMM [0135] 4.2.5. Preparation and Purification of hsp110-peptide complexes
[0139] 4.2.6. Preparation and Purification of grp170-peptide complexes
[0149] 4.2.10. Peptides from α -2m or hsp-peptide complexes
[0150] Antigenic molecules (e.g. peptides) can be eluted from hsp-antigenic molecule complexes either in the presence of ATP or low pH. Antigenic molecules can be eluted from α -2m-antigenic molecule complexes in the presence of low pH. These experimental conditions may be used to isolate peptides or non-peptide antigenic components from cells which may contain potentially useful antigenic determinants. Once isolated, the amino acid sequence of an antigenic peptide may be determined using conventional amino acid sequencing methodologies. Antigenic molecules can then be produced by chemical synthesis or recombinant.
- SUMM [0151] Thus, potentially immunogenic or antigenic peptides may be isolated from either endogenous stress protein-peptide complexes or endogenous MHC-peptide complexes for use subsequently as antigenic molecules, by complexing in vitro to hsp. While the low molecular weight may be analyzed by HPLC as described below. In the ATP incubation protocol, the stress protein-peptide complex in the large molecular weight fraction is incubated with 10 mM ATP for 30 minutes at room temperature. In the low pH protocol, acetic acid or trifluoroacetic acid (TFA) is added to the stress protein-peptide complex to give a final concentration of 10% (vol/vol) and the mixture incubated at room temperature or in a boiling.
- SUMM [0152] 10 assembly as mentioned previously. The high and low molecular weight fractions are recovered. The remaining large molecular weight stress protein-peptide complexes can be reincubated with ATP or low pH to remove any remaining peptides.
- SUMM [0153] by developing the column with a linear gradient of 0 to 80% acetonitrile in 0.1% TFA. The elution of the peptides can be monitored by OD, sub. 210 and the fractions containing the peptides collected.
- SUMM [0155] 4.2.11. Peptides from MHC-peptide complexes
[0156] The isolation of potentially immunogenic peptides from
- SUMM MHC molecules is well known in the art and so is not described in detail herein (See, Falk et al., J. Biol. Chem., 263:10761-10764, 1988).
- SUMM [0157] Briefly, MHC-peptide complexes may be isolated by a conventional immunofluorescence procedure. The peptides then may be eluted from the MHC-peptide complex by incubating the complexes in the presence of about 0.1% TFA in acetonitrile. The eluted peptides may be fractionated and purified by reverse phase HPLC, as before.
- SUMM [0158] The amino acid sequences of the eluted peptides may be determined either by manual or automated amino acid sequencing techniques well known in the art. Once the amino acid sequence of a potentially protective peptide has been determined the peptide may be synthesized in any desired amount using conventional peptide synthesis or other protocols well known in the art.
- SUMM [0159] peptides having the same amino acid sequence as those isolated above may be synthesized by solid-phase peptide synthesis using procedures similar to those described by Merrifield, 1963, J. Am. Chem. Soc. 85:2149. During synthesis, N α -protected amino acids are stepwise to a growing polypeptide chain linked by its C-terminal and to an insoluble polymeric support i.e., polystyrene beads. The peptides are synthesized by linking an amino group of an N α -protected amino acid to an α -carboxy group of an N α -protected amino acid with a reagent such as dicyclohexylcarbodiimide. The attachment of a free amino group to the activated carboxyl leads to peptide bond formation. The most commonly used N α -protecting groups include Boc which is acid labile and Fmoc which is base labile.
- SUMM [0160] is coupled to the activated α -carboxylate group of the next N α -protected amino acid. The process is repeated until the desired peptide is synthesized. The resulting peptides are then cleaved from the insoluble polymer support and the amino acid side chains deprotected. Longer peptides can be derived by condensation of protected peptide fragments. Details of appropriate chemistries, resins, protecting groups, protected amino acids and reagents are well known in the art and so are not discussed in detail herein (See, Atherton et al., 1989, Solid Phase Peptide Synthesis: A Practical Approach, IRL Press, and Bodanszky, 1993, Springer-Verlag).
- SUMM [0161] Purification of the resulting peptides is accomplished using conventional procedures, such as preparative HPLC using gel permeation, partition and/or ion exchange chromatography. The choice of.
- SUMM [0162] molecules associated with neurodegenerative diseases, or epitopes of antigenic molecules associated with amyloid diseases, including but not limited to fibril peptides or proteins, are used. For example, such neurodegenerative disease-associated antigenic molecules may be molecules associated with Alzheimer's Disease, age-related loss of proteins. Amyloid disease associated antigenic molecules may be molecules associated with diseases characterized by the extracellular deposition of protein and/or peptide fibrils which form amyloid deposits or plaques, including but not limited to type II diabetes and amyloidosis associated with chronic.
- SUMM [0173] In an embodiment in which complexes of hsp and the peptides with which they are endogenously associated in vivo are not employed, complexes of hsp to antigenic molecules are produced in vitro. As will be appreciated by those skilled in the art, the peptides either isolated by the aforementioned procedures or chemically synthesized or recombinantly produced may be reconstituted with a variety of purified.
- SUMM [0174] Prior to complexing, the hsp are pretreated with ATP or low pH to remove any peptides that may be associated with the hsp of interest. When the ATP procedure is used, excess ATP is removed from.

SUMM . . . mm phenyl methyl sulfonyl fluoride (PMSF). The preparations are centrifuged through a Centricon 10 assembly (Millipore) to remove any unbound peptide. The association of the peptides with the stress proteins can be assayed by SDS-PAGE. This is the preferred method for in vitro complexing of peptides isolated from MHC-peptide complexes of peptides disassociated from endogenous hsp-peptide complexes.

SUMM [0177] In an alternative embodiment of the invention, preferred for producing complexes of gp96 or hsp90 to peptides, 5-10 micrograms of purified gp96 or hsp90 is incubated with equimolar or excess quantities of the antigenic peptide in a suitable buffer such as one containing 20 mM sodium phosphate buffer pH 7.5, 0.5M NaCl, 3 mM MgCl₂. . . room temperature and centrifuged one or more times if necessary, through a Centricon 10 assembly (Millipore) to remove any unbound peptide.

SUMM [0182] Additional embodiments of the invention relate to pharmaceutical compositions comprising either .alpha.2M or an hsp, optionally a peptide (which need not be antigenic), and a saponin adjuvant, for the prevention or treatment of an autoimmune disorder. These compositions. . .

SUMM . . . the carboxyl group on the glucuronic acid of saponins from Quilaja saponaria Molina can be conjugated to a protein, a peptide, or a small molecule containing a primary amine. According to Higuchi et al., 1987, *Phytochemistry* 26:229, saponins from Quilaja saponaria. . .

SUMM . . . human patient) is applied at 20 degree. C. for 1 hour, and the plates are washed 3 times with PBS-T. The anti-peptide antibody activity is then measured calorimetrically after incubating at 20 degree. C. for 1 hour with 50 .mu.l/well of sheep anti-mouse. . .

SUMM . . . of this method, peripheral blood mononuclear cells from a subject treated with a composition of the invention are stimulated with peptide antigens of a given tumor or with peptide antigens of an agent of infectious disease. Cells are then stained with T cell-specific labeled antibodies detectable by flow cytometry. . .

SUMM . . . 274: 94-96) may be used to identify antigen-specific T-cells. For example, in one embodiment, an MHC molecule containing a specific peptide antigen, such as a tumor-specific antigen, is multimerized to make soluble peptide tetramers and labeled, for example, by complexing to streptavidin. The MHC-peptide antigen complex is then mixed with a population of T cells obtained from a subject treated with a composition of. . .

SUMM . . . be used to modify individual nucleotides in a DNA sequence, for purpose of making amino acid substitution(s) in the expressed peptide sequence, or for creating/deleting restriction sites to facilitate further manipulations. Such techniques include but are not limited to, chemical mutagenesis. . .

SUMM . . . incorporated herein by reference, demonstrates that deletion of the ER retention signal of gp96 results in the secretion of gp96-Ig peptide-complexes from transfected tumor cells, and that fusion of the KDEL-deleted gp96 with murine IgG1 facilitated its detection by ELISA and. . .

SUMM . . . be used to modify individual nucleotides in a DNA sequence, for purpose of making amino acid substitution(s) in the expressed peptide sequence, or for creating/deleting restriction sites to facilitate further manipulations. Such techniques include but are not limited to, chemical mutagenesis. . .

SUMM . . . incorporated herein by reference, demonstrates that deletion of the ER retention signal of gp96 results in the secretion of gp96-Ig peptide-complexes from transfected tumor cells, and that fusion of the KDEL-deleted gp96 with murine IgG1 facilitated its detection by ELISA and. . .

SUMM . . . polypeptide of any desired length can be generated using PCR primers that flank the nucleotide sequence encoding .alpha.2M, or the peptide-binding domain thereof. Alternatively, an .alpha.2M gene sequence can be cleaved at appropriate sites with restriction endonuclease(s) if such sites are available, releasing a fragment of DNA encoding .alpha.2M, or the peptidebinding domain thereof. If convenient restriction sites are not available, they may be created in the appropriate positions by site-directed mutagenesis. . . at (see, for example, Shankarappa et al., 1992, *PCR Method Appl.* 1:277-278). The

SUMM DNA fragment that encodes .alpha.2M, or the peptide-binding domain thereof, is then isolated, and ligated into an appropriate expression vector, care being taken to ensure that the proper. . .

SUMM . . . purification from the cells in which they are expressed. For example, an .alpha.2M polypeptide may contain a signal sequence leader peptide to direct its translocation across the ER membrane for secretion into culture medium. Further, an .alpha.2M polypeptide may contain an. . . affinity label, such as a .alpha.2M polypeptide, fused to any portion of the .alpha.2M polypeptide not involved in binding antigenic peptide, such as for example, the carboxyl terminal. The affinity label can be used to facilitate purification of the protein, by. . .

SUMM . . . frame into a vector containing the sequence of an affinity label, such that the .alpha.2M polypeptide is expressed as a peptide-tagged fusion protein. Affinity labels, which may be recognized by specific binding partners, may be used for affinity purification of the. . .

SUMMalpha.2M polypeptide novel structural properties, such as the ability to form multimers. Dimerization of an .alpha.2M polypeptide with a bound peptide may increase avidity of interaction between the .alpha.2M polypeptide and its partner in the course of antigen presentation. These affinity. . .

SUMM . . . involved in disulfide bonding with other cysteines in the Ig molecule. Since none of the cysteines are required for the peptide to function as a tag, one or more of these cysteine residues may optionally be substituted by another amino acid. . .

SUMM . . . for the efficient secretion of .alpha.2M polypeptide from bacterial and mammalian cells (von Heijne, 1985, *J. Mol. Biol.* 184:99-105). Leader peptides are selected based on the intended host cell, and may include bacterial, yeast, viral, animal, and mammalian sequences. For example, the herpes virus glycoprotein D leader peptide is suitable for use in a variety of mammalian cells. A preferred leader peptide for use in mammalian cells can be obtained from the V-12-C region of the mouse immunoglobulin kappa chain (Bernard et al. . .

SUMM [0261] DNA sequences encoding a desired affinity label or leader peptide, which may be readily obtained from libraries, produced synthetically, or may be available from commercial suppliers, are suitable for the. . .

SUMM [0272] For long-term, high-yield production of properly processed hsp-peptide complexes, stable expression in mammalian cells is preferred. Cell lines that stably express hsps or .alpha.2M and antigenic molecules to produce hsp-peptide complexes for incorporating into the compositions of the present invention may be engineered by using a vector that contains a. . .

SUMM . . . repeat (LTR), a 3' LTR, a packaging signal, a bacterial origin of replication, and a selectable marker. The ND-associated antigenic peptide DNA is inserted into a position between the 5' LTR and 3' LTR, such that transcription from the 5' LTR. . .

SUMM . . . of the present invention include but are not limited to are diseases characterized by the extracellular deposition of protein and/or peptide fibrils which form amyloid deposits or plaques, including but not limited to type II diabetes and amyloidoses associated with chronic. . .

SUMM . . . done prior to administration, before or after the compositions of the invention are formulated. Wherein covalent complexing of an endogenous hsp-peptide complex is desired, the complex is preferably cross-linked after purification from cells or tissues. In one embodiment, antigenic molecules are. . . in a preferred embodiment, glutaraldehyde crosslinking may be used. Glutaraldehyde crosslinking has been used for formation of covalent complexes of peptides and hsps (see Barrios et al., 1992, *Eur. J. Immunol.* 22: 1365-1372). Preferably, 1-2 mg of complex is crosslinked in. . .

SUMM . . . adoptive immunotherapy using APC sensitized with hsp- or .alpha.2M-antigenic molecule complexes. As described in Section 4.10

herein, the hsp- or α -2M-peptide complex-sensitized APC can be administered alone, in combination claimed compositions, or before or after administration of the claimed compositions. Furthermore, . . .

15 minutes to 24 hours. By way of example but not limitation, 4 times 10⁶ macrophages can be incubated with 10 microgram gp96-peptide complexes per ml or 100 microgram hsp90-peptide complexes per ml at 37 degree C. for 15 minutes-24 hours in 1 ml plain RPMI medium. The cells are washed.

of a putative biomarker for risk of a specific cancer are measured to monitor the effect of hsp bound to peptide complexes. For example, in individuals at enhanced risk for prostate cancer, serum prostate-specific antigen molecule (PSA) is measured by the . . .

will be understood that, where reference is made to an antigenic molecule as a component of a composition, an antigenic peptide or full-length protein may be used (e.g. having more than 50 amino acid residues). The amount of an antigenic molecule. . .

day interval, either (i) phosphate buffer saline (PBS), (ii) peptide complexes derived from U6139SJ carcinomas, or (iii) 0.1, 1, 10, 25, 50, or 100 μ g/mouse of, for example, gp96-peptide complexes derived from U6139SJ carcinomas, or (iii) 0.1, 1, 10, 25, 50, or 100 μ g/mouse of gp96-peptide complexes derived from U6139SJ carcinoma. For each dosage of gp96-peptide complex, 0.1, 1, 10, 20, 50, or 100 μ g of saponin fraction QS-21 (reconstituted in PBS from lyophilized powder) is mixed with the gp96-peptide complexes and administered. Control sets of mice receive the dosage series of QS-21 alone.

(10391) Coadministration of one or more saponins along with gp96-peptide complexes will elicit the desired immune response using reduced levels of the gp96-peptide complexes as compared to gp96-peptide complexes administered alone (i.e. in the absence of saponin). Accordingly, the invention provides the advantage of permitting reduction of the amount of an hsp or α -2M-peptide complex required to elicit a desired immune response for prevention or treatment of cancer or infectious disease.

a second group receive, every other day for a total of five injections, 6, 1, 0.6, or 0.1 μ g/mouse of gp96-peptide complex derived from U6139SJ carcinoma cells. Mice in a third group receive, in a similar manner, a total of five injections of gp96-peptide complex derived from normal liver. Mice in a fourth group receive, in a similar manner, a total of five injections of gp96-peptide complex derived from the U6139SJ carcinoma cells, mixed with 20 or 100 μ g of QS-21. The mice in the fifth group receive, in a similar manner, a total of five injections of gp96-peptide complex derived from normal liver mixed with 20 or 100 μ g QS-21. Finally, the mice in the sixth group receive. . .

the liver-derived gp96 or in untreated mice (see U.S. Pat. No. 5,837,251). These results indicated a therapeutic effect of gp96 peptide complexes in the U6139SJ carcinoma model. All mice eventually succumbed to tumor growth. A scrutiny of the kinetics of tumor growth in treated and control mice shows that administration of tumor-derived gp96-peptide complex had an immediate inhibitory effect on tumor growth and that the effect appears to diminish after treatment with gp96-peptide complex is terminated.

(10403) Coadministration of QS-21 with gp96-peptide complex derived from U6139SJ carcinoma cells will result in a retardation of tumor growth when using smaller amounts of gp96-peptide complex as compared to the group receiving gp96-peptide complex from U6139SJ carcinoma cells without QS-21. The administration of QS-21 alone, or gp96-peptide complex from normal liver plus QS-21, will not result in any significant difference as compared to the PBS control, or gp96-peptide complex from normal liver, respectively.

growth of established tumors using reduced amounts of the hsp

or α -2M when saponin adjuvant is present. Additionally, recombinantly-expressed antigenic peptide - α -2M or -hsp fusion proteins can also be employed to elicit immunosuppression of new tumors and retarded growth of established. . .

What is claimed is:
1. A pharmaceutical composition comprising a purified heat shock protein (hsp) and a saponin.

=> d his

(FILE 'HOME' ENTERED AT 15:25:49 ON 20 FEB 2003)

FILE 'MEDLINE, CANCERLIT, BIOSIS, CONSCI, EMBASE, CAPLUS, USPATFULL'
ENTERED AT 15:26:27 ON 20 FEB 2003
72563 S HEAT (A) SHOCK (A) PROTEIN
40 S L1 AND ALPHA (A) 2 (A) MACROGLOBULIN (A) RECEPTOR
L2 33 DUP REM L2 (7 DUPLICATES REMOVED)
L3 12721 S L1 AND ANTIBODY
L4 21 S L4 AND L2
L5 19 DUP REM L5 (2 DUPLICATES REMOVED)
L6 1585 S ACONISTY AND L1
L7 4 S L7 AND L2
L8 8637 S L1 AND PEPTIDE
L9 27 S L9 AND L2
L10 24 DUP REM L10 (3 DUPLICATES REMOVED)
L11 11 S L11 AND MODULATE?
L12

=> s alpha (a) 2 (a) macroglobulin (a) receptor
L13 1624 ALPHA (A) 2 (A) MACROGLOBULIN (A) RECEPTOR

=> s l13 and modulate?
L14 160 L13 AND MODULATE?

=> dup rem l14
PROCESSING COMPLETED FOR L14
L15 110 DUP REM L14 (50 DUPLICATES REMOVED)

=> s l15 and heat (a) shock (a) protein
6 FILES SEARCHED...
L16 14 L15 AND HEAT (A) SHOCK (A) PROTEIN

=> d 1-14

L16 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2003 ACS
AN 2002:937303 CAPLUS
DN 138:20443
TI Endocrine disruptor screening using DNA chips of endocrine
disruptor-responsive genes
IN Kondo, Akhiro, Takeda, Takeshi; Mizutani, Shigetoshi; Tajimoto,
Yoshimasa; Takashima, Ryokichi; Enoki, Yuki; Kato, Ikunobu
PA Takara Bio Inc., Japan
SO Jpn. Kokai Tokkyo Koho, 386 pp.
CODEN: JKKXAF

DT Patent
LA Japanese
FAN: CMT 1

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JP 2001-73183	A	20010314		
JP 2001-74993	A	20010315		
JP 2001-102519	A	20010330		

L16 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2003 ACS
AN 2001:886449 CAPLUS
DN 136:36328
TI Alpha 2 macroglobulin receptors as
a heat shock protein receptor and uses
thereof
IN Strivastava, Pramod K.
PA University of Connecticut Health Center, USA
SO PCT Int. Appl., 236 pp.
DT Patent
LA English
FAN CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE
PI WO 2001092474 A1 20011206 WO 2001-US18041 20010604
W: AU, CA, JP
RM: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, TR

PRAI US 2000-209095P P 20000602
US 2000-625137 A 20000725
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US 2000-750972 A 20001228
RE CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2003 ACS
AN 2001:851435 CAPLUS
DN 136:1570
TI Compositions, kits, and methods for identification and modulation
of T helper-1 and T helper-2 cells and diseases associated therewith
IN Hanrahan, Catherine F.; Feldman, Marc; Trepicchio, William L.
PA Genetics Institute, Inc., USA, Kennedy Institute of Rheumatology
SO PCT Int. Appl., 115 pp.
DT Patent
LA English
FAN CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE
PI WO 2001088199 A2 20011122 WO 2001-US16022 20010517
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GR, GD, GE, GH,
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LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, NO, NZ, PL, PT,
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US 2002039734 A1 20020404 US 2001-860655 20010517
PRAI US 2000-205204P P 20000518

L16 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2003 ACS
AN 2001:763235 CAPLUS
DN 135:314399
TI Detection of variations in the DNA methylation profile of genes in the
determining the risk of disease
IN Berlin, Kurt; Piepenbrock, Christian; Olek, Alexander
PA Epigenomics A.-G., Germany
SO PCT Int. Appl., 636 pp.
DT Patent
LA German
FAN CNT 68

PATENT NO. KIND DATE APPLICATION NO. DATE
PI WO 200107373 A2 20011018 WO 2001-DE1486 20010406
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DE 10019058 A1 20011220 DE 2000-10019058 20000406
WO 200107373 A2 20011018 WO 2001-XA1486 20010406
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CF, CG, CI, CM, CN, CU, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
WO 200107373 A2 20011018 WO 2001-XB1486 20010406
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ZW, AM, AZ, BY, BG, BR, BY, BZ, CA, CH, CN, CY,
RM: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
CF, CG, CI, CM, CN, CU, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
EP 1274865 A2 20030115 EP 2001-95356 20010406
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, EP 2001-940158 20010406
EP 1274865 A1 20030129 EP 2001-940158 20010406
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, EP 2001-940158 20010406
PRAI DE 2000-10019058 A 20000406
DE 2000-10019058 A 20000406
DE 2000-10032529 A 20000630
DE 2000-10043826 A 20000901
WO 2001-DE1486 W 20010406
WO 2001-EP3969 W 20010406

L16 ANSWER 5 OF 14 USPATFULL
AN 2003:40533 USPATFULL
TI Methods for the inhibition of Epstein-Barr virus transmission employing
anti-viral peptides capable of abrogating viral fusion and transmission
IN Lambert, Dennis Michael; Cary, NC, United States
Patteway, Stephen Robert; Cary, NC, United States
Timmeria, Inc., Durham, NC, United States (U.S. corporation)
PA US 6518013 B1 20030211
FI US 1995-485546 19950607 (8)
R1 Continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994,
now patented. Pat. No. US 6017536 Continuation-in-part of Ser. No. US
1994-255208, filed on 7 Jun 1994 Continuation-in-part of Ser. No. US
1993-73028, filed on 7 Jun 1993, now patented. Pat. No. US 5464933
utility
DT GRANTED
FS 24700
INCL INCLM: 435/005.000
INCLS: 424/230.100; 530/300.000; 530/324.000; 530/325.000; 530/326.000

NCL NCLM: 435/005.000
NCLS: 424/230.100; 530/300.000; 530/324.000; 530/325.000; 530/326.000

IC [7]
ICM: C120001-70

EXF 435/5; 435/300; 530/324-329; 530/350; 424/230.1

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 6 OF 14 USPATFULL
AN 2002:315069 USPATFULL
TI Compositions and methods for treatment of neoplastic disease
PI Teram, David S., Pebble Beach, CA, UNITED STATES
IN US 2002177551 A1 20021128
AI US 2001-870759 A1 20010530 (9)
PRAI US 2000-208128P 20000531 (60)
DT Utility
FS APPLICATION

LN.CNT 17323
INCL INCLM: 514/012.000
NCLS: 435/325.000; 530/350.000
NCLM: 514/012.000
NCLS: 435/325.000; 530/350.000

IC [7]
ICM: A61K038-17

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 7 OF 14 USPATFULL
AN 2002:297296 USPATFULL
TI Methods for inhibition of membrane fusion-associated events, including respiratory syncytial virus transmission
IN Bolognesi, Dan Paul, Durham, NC, United States
Matthews, Thomas James, Durham, NC, United States
Wild, Carl T., Durham, NC, United States
Barney, Shawn O'Lin, Cary, NC, United States
Lambert, Dennis Michael, Cary, NC, United States
Petterway, Stephen Robert, Cary, NC, United States
Langlois, Alphonse J., Durham, NC, United States
Triemeris, Inc., Durham, NC, United States (U.S. corporation)
PI US 6478055 B1 20021112
AI US 1993-470896 19950606 (8)
Continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994, now patented, Pat. No. US 6017536 Continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994 Continuation-in-part of Ser. No. US 1993-73028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933

DT Utility
FS GRANTED

LN.CNT 26553
INCL INCLM: 424/211.100
NCLS: 424/186.100; 530/324.000
NCLM: 424/211.100
NCLS: 424/186.100; 530/324.000

IC [7]
ICM: A61K039-145

EXF 435/5; 435/240.2; 424/184.1-189.1; 424/204.1-211.1; 424/225.1; 424/227.1; 424/230.1; 514/1; 514/2; 530/324; 530/350; 530/826

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 8 OF 14 USPATFULL
AN 2002:259381 USPATFULL
TI Materials and methods relating to lipid metabolism
IN Ballinger, Dennis G., Menlo Park, CA, UNITED STATES
Loeb, Deborah, San Jose, CA, UNITED STATES
Montgomery, Julie R., Santa Cruz, CA, UNITED STATES
Tang, Y. Tom, San Jose, CA, UNITED STATES
Zhou, Ping, Cupertino, CA, UNITED STATES

Goodrich, Ryle, San Jose, CA, UNITED STATES
Liu, Chenghua, San Jose, CA, UNITED STATES
Asundi, Vinod, Foster City, CA, UNITED STATES
Zhao, Qing A., San Jose, CA, UNITED STATES
Webman, Tom, Stanford, CA, UNITED STATES
Dmanac, Radoje T., Palo Alto, CA, UNITED STATES
Ren, Feiyan, Cupertino, CA, UNITED STATES
Qian, Xiaohong B., San Jose, CA, UNITED STATES
Wang, Duntui, Poway, CA, UNITED STATES
US 2002142953 A1 20010416 (9)
US 2001-835996 A1 20010416 (9)
Continuation-in-part of Ser. No. US 2000-714936, filed on 17 Nov 2000, PENDING Continuation-in-part of Ser. No. US 2000-667298, filed on 22 Sep 2000, PENDING Continuation-in-part of Ser. No. US 2000-631451, filed on 3 Aug 2000, PENDING Continuation-in-part of Ser. No. US 2000-598042, filed on 20 Jun 2000, PENDING

PRAI US 2000-197137P 20000414 (60)
DT Utility
FS APPLICATION

LN.CNT 9120
INCL INCLM: 514/012.000
NCLS: 435/069.100; 435/325.000; 435/320.100; 530/359.000; 435/196.000; 536/023.200
NCLM: 514/012.000
NCLS: 435/069.100; 435/325.000; 435/320.100; 530/359.000; 435/196.000; 536/023.200

IC [7]
ICM: A61K038-17

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 9 OF 14 USPATFULL
AN 2002:206116 USPATFULL
TI Toxicant-induced differential gene expression
IN Reidhaar-Olson, John F., Montclair, NJ, UNITED STATES
PI US 2002110808 A1 20020815
AI US 2000-489220 A1 20000121 (9)
DT Utility
FS APPLICATION

LN.CNT 5161
INCL INCLM: 435/006.000
NCLS: 435/091.200; 536/023.100
NCLM: 435/006.000
NCLS: 435/091.200; 536/023.100

IC [7]
ICM: C120001-68

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 10 OF 14 USPATFULL
AN 2002:164658 USPATFULL
TI Immunotherapeutic methods for extracorporeal modulation of CD36 and its ligands
IN Srivastava, Pramod K., Avon, CT, UNITED STATES
PI US 2002086276 A1 20020704
AI US 2000-750973 A1 20001228 (9)
DT Utility
FS APPLICATION

LN.CNT 1813
INCL INCLM: 435/002.000
NCLS: 424/140.100
NCLM: 435/002.000
NCLS: 424/140.100

IC [7]
ICM: A61K039-395

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 11 OF 14 USPATFUL
 AN 2002:136555 USPATFUL
 TI Methods of modulating an immune response to antigen, and cells
 for use in the method
 IN Segal, Andrew H., Boston, MA, United States
 PA Whitehead Institute for Biomedical Research, Cambridge, MA, United
 States (U.S. corporation)
 PI US 6403080 B1 20020611
 AI US 1999-339523 19990624 (9)
 RLI Division of Ser. No. US 1997-826259, filed on 27 Mar 1997, now patented,
 Pat. No. US 5951976
 PRAI US 1996-14364P 19960328 (60)
 PS Utility
 DT Granted
 LN.CNT 2153
 INCL INCLM: 424/093.100
 INCLS: 424/093.200; 424/093.210; 424/093.700; 424/093.710; 424/136.100;
 435/325.000; 514/002.000; 514/012.000; 530/387.300
 NCLM: 424/093.100
 NCLS: 424/093.200; 424/093.210; 424/093.700; 424/093.710; 424/136.100;
 435/325.000; 514/002.000; 514/012.000; 530/387.300
 IC [7]
 ICM: A01N063-00
 EXF ICS: A61K039-395; A61K038-00; C12P021-08
 424/93.21; 424/93.71; 424/93.1; 424/93.2; 424/93.71; 424/136.1; 435/325;
 514/12; 514/21; 530/387.3
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 12 OF 14 USPATFUL
 AN 2002:66639 USPATFUL
 TI Compositions comprising heat shock proteins
 or alpha(2) macroglobulin, antigenic molecules and saponins, and methods
 of use thereof
 IN Armen, Gary H., Mahanassett, NY, UNITED STATES
 PI US 200207290 A1 20020328
 AI US 2001-309778 A1 20010720 (9)
 PRAI US 2000-223133P 20000807 (60)
 DT Utility
 FS APPLICATION
 LN.CNT 4136
 INCL INCLM: 424/178.100
 INCLS: 514/012.000; 514/026.000
 NCLM: 424/178.100
 NCLS: 514/012.000; 514/026.000
 IC [7]
 ICM: A61K039-395
 ICS: A61K038-17
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 13 OF 14 USPATFUL
 AN 2001:67794 USPATFUL
 TI Human respiratory syncytial virus peptides with antitumor and
 antiviral activities
 IN Barney, Shawn O'Din, Cary, NC, United States
 Lambert, Dennis Michael, Cary, NC, United States
 Petterway, Stephen Robert, Cary, NC, United States
 Trimeris, Inc., Durham, NC, United States (U.S. corporation)
 PI US 628993 B1 20010508
 AI US 1995-485264 19950607 (8)
 RLI Division of Ser. No. US 1995-470896, filed on 6 Jun 1995
 Continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994
 Continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994
 Continuation-in-part of Ser. No. US 1993-73028, filed on 7 Jun 1993, now

patented, Pat. No. US 5464933

DT Utility
 PS Granted
 LN.CNT 32166
 INCL INCLM: 530/300.000
 INCLS: 530/324.000; 530/325.000; 530/326.000; 424/211.100; 424/186.100
 NCLM: 530/300.000
 NCLS: 424/186.100; 424/211.100; 530/324.000; 530/325.000; 530/326.000
 IC [7]
 ICM: A61K038-00
 EXF 530/350; 530/324-329; 530/300; 424/211.1
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 14 OF 14 USPATFUL
 AN 1999:141305 USPATFUL
 TI Adjuvant for transcutaneous immunization
 IN Glenn, Gregory M., Bethesda, MD, United States
 Alving, Carl R., Bethesda, MD, United States
 PA The United States of America as represented by the U.S. Army Medical
 Research & Materiel Command, Washington, DC, United States (U.S.
 government)
 PI US 5980898 19991109
 AI US 1997-896085 19970717 (8)
 RLI Continuation-in-part of Ser. No. US 1996-749164, filed on 14 Nov 1996
 DT Utility
 PS Granted
 LN.CNT 1988
 INCL INCLM: 424/184.100
 INCLS: 424/449.000; 424/450.000; 424/236.000; 424/240.100; 424/241.100;
 424/275.100; 530/363.000; 530/403.000
 NCLM: 424/184.100
 NCLS: 424/085.100; 424/240.100; 424/241.100; 424/275.100; 424/449.000;
 424/450.000; 530/363.000; 530/403.000
 IC [6]
 ICM: A61K039-00
 ICS: C07K014-005; C07K014-195
 EXF 424/449; 424/450; 424/184.1; 424/236; 424/240.1; 424/241.1; 424/275.1;
 530/363; 530/403
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d his

(FILE 'HOME' ENTERED AT 15:25:49 ON 20 FEB 2003)

FILE 'MEDLINE, CANCERLIT, BIOSIS, CONFSCI, EMBASE, CAPLUS, USPATFUL.'
 ENTERED AT 15:26:27 ON 20 FEB 2003

L1 72563 S HEAT (A) SHOCK (A) PROTEIN
 L2 40 S L1 AND ALPHA (A) 2 (A) MACROGLOBULIN (A) RECEPTOR
 L3 33 DUP REM L2 (7 DUPLICATES REMOVED)
 L4 12721 S L1 AND ANTIBODY?
 L5 21 S L4 AND L2
 L6 19 DUP REM L5 (2 DUPLICATES REMOVED)
 L7 1585 S ACONIST? AND L1
 L8 4 S L7 AND L2
 L9 8637 S L4 AND PEPTIDE?
 L10 27 S L9 AND L2
 L11 24 DUP REM L10 (3 DUPLICATES REMOVED)
 L12 11 S L11 AND MODULATE?
 L13 1624 S ALPHA (A) 2 (A) MACROGLOBULIN (A) RECEPTOR
 L14 160 S L13 AND MODULATE?
 L15 110 DUP REM L14 (50 DUPLICATES REMOVED)
 L16 14 S L15 AND HEAT (A) SHOCK (A) PROTEIN

=> s 114 and peptid?

LA	ANSWER OF 50 CAPLUS	COPYRIGHT 2003 ACS	
DN	2002-888494	CAPLUS	
TI	137-381503		
IN	Compositions and methods for modulating Dlx-mediated protein interactions and their diagnostic and therapeutic uses		
PA	Allen, Kristina; Antkowiak, Anthony; Bhat, Bheem M.; Dannaegre, Veronique; Robinson, John Allen; Yavorsky, Paul J.		
SO	Genome Therapeutics Corporation, USA; Wyeth, John and Brother Ltd.		
DT	PCT Int. Appl., 376 pp.		
LA	English		
PAT	PATENT NO.	KIND	DATE
PI	WO 2002/0292015	A2	20021121
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NO, NZ, OM, PA, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, AY, BK, BZ, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, MD, ME, NE, SN, TG, TM		
PRAI	US 2001-291311	P	20010517
US	2002-353058P	P	20020521
US	2002-361293P	P	20020304
L18	ANSWER 8 OF 50 CAPLUS	COPYRIGHT 2003 ACS	
DN	2002-736374	CAPLUS	
TI	137-259633		
IN	Protein-protein interactions of CLIC1 and diagnosis and treatment of proinflammatory immune response and other diseases		
PA	Cimpora, Daniel M.; Heichman, Karen; Bartel, Paul L.		
SO	Myriad Genetics, Inc., USA		
DT	PCT Int. Appl., 47 pp.		
LA	English		
PAT	PATENT NO.	KIND	DATE
PI	WO 2002/074319	A2	20020926
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NO, NZ, OM, PA, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, AY, BK, BZ, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, MD, ME, NE, SN, TG, TM		
PRAI	US 2002197626	A1	20020315
US	2002197626	A1	20020315
PRAI	US 2001-376037P	P	20010316
L18	ANSWER 9 OF 50 CAPLUS	COPYRIGHT 2003 ACS	
DN	2002-89853	CAPLUS	
TI	136-14528		
IN	Methods for the treatment of neuro, disorders with agents that bind to low-d, lipoprotein receptor-related protein receptors		
PA	Hyman, Bradley T.; Strickland, Dudley K.; Backst, Brian J.; Rebeck, G. William		
SO	The General Hospital Corporation, USA; The American National Red Cross		

SO PCT Int. Appl., 50 PP.
 DT Patent
 LA English
 FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 2002007755 A1 20020131 WO 2000-US40636 20000815

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TW, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, BG, BR, CA, CH, CN, CU, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GN, GW, ML, MR, NE, SN, TD, TG

RW: GH, GM, KE, LS, MM, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-220439 P 20000724
 RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 10 OF 50 CAPLUS COPYRIGHT 2003 ACS
 AN 2002:850252 CAPLUS
 DN 137:363083

TI Methods of suppressing microglial activation by administering compounds binding to microglial receptors

IN Leikowitz, Daniel T.; Matthew, William D.; McMillian, Michael

PA U.S. Pat. Appl. Publ., 25 pp., Cont.-in-part of U. S. Ser. No. 260,430.

SO CODEN: USXXCO

DT Patent
 LA English
 FAN.CNT 2

PATENT NO. KIND DATE APPLICATION NO. DATE

PI US 2002164789 A1 20021107 US 2001-957909 20010921
 PRAI US 1998-77551P P 19980311
 US 1999-260430 A2 19990301

L18 ANSWER 11 OF 50 CAPLUS COPYRIGHT 2003 ACS
 AN 2002:937303 CAPLUS
 DN 138:20443

TI Endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes

IN Kondo, Akihiro; Takeda, Takeshi; Mizutani, Shigetoshi; Tsujimoto, Yoshinaga; Takashima, Ryokichi; Enoki, Yuki; Kato, Ikumoshin

PA Takara Bio Inc., Japan
 SO Jpn. Kokai Tokkyo Koho, 386 pp.
 CODEN: JCKXAF

DT Patent
 LA Japanese
 FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI JP 2002355079 A2 20021210 JP 2002-69354 20020313
 PRAI JP 2001-73183 A 20010315
 JP 2001-74993 A 20010315
 JP 2001-102519 A 20010330

L18 ANSWER 12 OF 50 USPATFULT
 AN 2002:315069 USPATFULT
 TI Compositions and methods for treatment of neoplastic disease
 IN Terman, David S.; Pebble Beach, CA, UNITED STATES
 PI US 2002177551 A1 20021128
 US 2001-870759 A1 20010530 (9)

PRAI US 2000-208128P 20000531 (60)
 DT Utility
 FS APPLICATION
 LN.CNT 17323

INCL INCLM: 514/012.000
 INCLS: 435/325.000, 530/350.000
 NCLM: 514/012.000
 NCLM: 435/325.000, 530/350.000

IC [7]
 ICM: A61K038-17
 ICS: C07H021-04, C12N009-16, C12P021-02, C12N005-06; C07K014-775
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 13 OF 50 USPATFULT
 AN 2002:259381 USPATFULT
 TI Materials and methods relating to lipid metabolism

IN Leob, Deborah; San Jose, CA, UNITED STATES
 Ballinger, Dennis G.; Menlo Park, CA, UNITED STATES
 Loeb, Deborah; San Jose, CA, UNITED STATES
 Tang, Y. Tom; San Jose, CA, UNITED STATES
 Montgomery, Julie R.; Santa Cruz, CA, UNITED STATES
 Zhou, Ping; Cupertino, CA, UNITED STATES
 Goodrich, Ryle; San Jose, CA, UNITED STATES
 Liu, Chenghua; San Jose, CA, UNITED STATES
 Asundi, Vinod; Foster City, CA, UNITED STATES
 Zhao, Qing A.; San Jose, CA, UNITED STATES
 Weinman, Tom; Stanford, CA, UNITED STATES
 Dermanac, Radoje T.; Palo Alto, CA, UNITED STATES
 Ren, Feiyun; Cupertino, CA, UNITED STATES
 Qian, Xiaohong B.; San Jose, CA, UNITED STATES
 Wang, Duntui; Poway, CA, UNITED STATES

PI US 2001-835996 A1 20010416 (9)
 US 2001-835996 A1 20010416 (9)
 US 2001-835996 A1 20010416 (9)

RII Continuation-in-part of Ser. No. US 2000-714936, filed on 17 Nov 2000, PENDING Continuation-in-part of Ser. No. US 2000-667298, filed on 22 Sep 2000, PENDING Continuation-in-part of Ser. No. US 2000-631451, filed on 3 Aug 2000, PENDING Continuation-in-part of Ser. No. US 2000-598042, filed on 20 Jun 2000, PENDING

PRAI US 2000-197137P 20000414 (60)
 DT Utility
 FS APPLICATION
 LN.CNT 9120

INCL INCLM: 514/012.000
 INCLS: 435/069.100, 435/325.000, 435/320.100, 530/359.000, 435/196.000;
 NCLM: 514/012.000
 NCLM: 435/069.100, 435/325.000, 435/320.100, 530/359.000, 435/196.000;
 NCLM: 514/012.000

IC [7]
 ICM: A61K038-17
 ICS: C07H021-04, C12N009-16, C12P021-02, C12N005-06; C07K014-775
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 14 OF 50 USPATFULT
 AN 2002:242784 USPATFULT
 TI Compositions and methods for modulating muscle cell and tissue contractility

IN Cines, Douglas B.; Wynnewood, PA, UNITED STATES
 Higazi, Adal A.; Jerusalem, ISRAEL
 PA The Trustees of the University of Pennsylvania (U.S. corporation)
 PI US 2002131964 A1 20020919
 US 2001-880503 A1 20010613 (9)
 PRAI US 2000-212874P 20000620 (60)
 DT Utility
 FS APPLICATION
 LN.CNT 3572

INCL INCLM: 424/094.630
NCL NCLM: 424/094.630
IC [7]
ICM: A61K038-48
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 15 OF 50 USPATFUL
AN 2002:206116 USPATFUL
TI Toxicant-induced differential gene expression
IN Reihart-Olson, John F., Montclair, NJ, UNITED STATES
PI US 2002110808 AI 20020815
AI US 2000-489220 AI 20000121 (9)
DT Utility
FS APPLICATION
LN.CNT 5161
INCL INCLM: 435/006.000
NCL INCLM: 435/091.200; 536/023.100
NCLM: 435/006.000
NCLS: 435/091.200; 536/023.100
IC [7]
ICM: C120001-68
ICS: C07H021-02; C07H021-04; C12P019-34
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 16 OF 50 USPATFUL
AN 2002:164658 USPATFUL
TI Immunotherapeutic methods for extracellular modulation of
CD36 and its ligands
IN Sriastava, Pramod K., Avon, CT, UNITED STATES
PI US 2002068276 AI 20020704
AI US 2000-750973 AI 20001228 (9)
DT Utility
FS APPLICATION
LN.CNT 1813
INCL INCLM: 435/002.000
NCL INCLM: 424/140.100
NCLM: 435/002.000
NCLS: 424/140.100
IC [7]
ICM: A61K039-395
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 17 OF 50 USPATFUL
AN 2002:105967 USPATFUL
TI Complex for transferring an anionic substance of interest into a cell
IN Rittner, Karola, Strasbourg, FRANCE
PI US 2002055174 AI 20020509
AI US 2001-865553 AI 20010529 (9)
PRAI EP 2000-440162 20000526
EP 2001-440049 20010227
US 2000-246083P 20001107 (60)
US 2001-277982P 20010323 (60)
DT Utility
FS APPLICATION
LN.CNT 1919
INCL INCLM: 435/463.000
NCL INCLM: 530/350.000
NCLM: 435/463.000
NCLS: 530/350.000
IC [7]
ICM: C12N015-87
ICS: C07K014-00
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 18 OF 50 USPATFUL
AN 2002:66639 USPATFUL
TI Compositions comprising heat shock proteins or alpha(2) macroglobulin,
antigenic molecules and saponins, and methods of use thereof
IN Armen, Garo H., Manhasset, NY, UNITED STATES
PI US 2002037290 AI 20020328
AI US 2001-909778 AI 20010720 (9)
PRAI US 2000-223133P 20000807 (60)
DT Utility
FS APPLICATION
LN.CNT 4136
INCL INCLM: 424/178.100
NCL INCLM: 514/012.000; 514/026.000
NCLM: 424/178.100
NCLS: 514/012.000; 514/026.000
IC [7]
ICM: A61K039-395
ICS: A61K038-17
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 19 OF 50 USPATFUL
AN 2002:297296 USPATFUL
TI Methods for inhibition of membrane fusion-associated events, including
respiratory syncytial virus transmission
IN Bolognesi, Dani Paul, Durham, NC, United States
Matthews, Thomas James, Durham, NC, United States
Wald, Carl T., Durham, NC, United States
Barney, Shawn O'Lin, Cary, NC, United States
Lambert, Dennis Michael, Cary, NC, United States
Petteley, Stephen Robert, Cary, NC, United States
Langlois, Alphonse J., Durham, NC, United States
Trimeris, Inc., Durham, NC, United States (U.S. corporation)
PI US 6479055 BI 20021112
AI US 1995-470896 19950606 (8)
RI Continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994,
now patented, Pat. No. US 6017535 Continuation-in-part of Ser. No. US
1994-255208, filed on 7 Jun 1994 Continuation-in-part of Ser. No. US
1993-73028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933
DT Utility
FS GRANTED
LN.CNT 26553
INCL INCLM: 424/211.100
NCL INCLM: 424/186.100; 530/324.000
NCLM: 424/211.100
NCLS: 424/186.100; 530/324.000
IC [7]
ICM: A61K039-145
EXF 435/5; 435/240.2; 424/184.1-189.1; 424/204.1-211.1; 424/225.1;
424/227.1; 424/230.1; 514/1; 514/2; 530/324; 530/350; 530/826
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 20 OF 50 USPATFUL
AN 2002:136555 USPATFUL
TI Methods of modulating an immune response to antigen, and cells
for use in the method
IN Segal, Andrew H., Boston, MA, United States
PA Whitehead Institute for Biomedical Research, Cambridge, MA, United
States (U.S. corporation)
PI US 6403080 BI 20020611
AI US 1999-339523 19990624 (9)
RI Division of Ser. No. US 1997-826259, filed on 27 Mar 1997, now patented,
Pat. No. US 5951976
PRAI US 1996-14364P 19960328 (60)
DT Utility
FS GRANTED

LN CNT 2153
INCL INCLM: 424/093.100
INCLM: 424/093.200; 424/093.210; 424/093.700; 424/093.710; 424/136.100;
435/325.000; 514/002.000; 514/012.000; 530/387.300
NCLM: 424/093.100
NCLM: 424/093.200; 424/093.210; 424/093.700; 424/093.710; 424/136.100;
435/325.000; 514/002.000; 514/012.000; 530/387.300
IC [7]
ICM: A01N063-00
ICS: A61K038-00; C12P021-08
424/093.21; 424/093.7; 424/093.1; 424/093.2; 424/093.71; 424/136.1; 435/325;
514/12; 514/21; 530/387.3
EXP 514/12; 514/21; 530/387.3
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L18 ANSWER 21 OF 50 USPTAFULL
AN 2002.19393 USPTAFULL
TI Secreted protein HLMFP03
IN Rosen, Craig A., Laytonville, MD, United States
Ruben, Steven M., Olney, MD, United States
Olsen, Henrik S., Galtersburg, MD, United States
Ebner, Reinhard, Galtersburg, MD, United States
Human Genome Sciences, Inc., Rockville, MD, United States (U.S.
corporation)
PI US 6342581 B1 20020129
AI US 1999-227357 19990108 (9)
R1 Continuation-in-part of Ser. No. WO 1998-US13684, filed on 7 Jul 1998
PRAI US 1997-58785P 19970912 (60)
US 1997-58664P 19970912 (60)
US 1997-58660P 19970912 (60)
US 1997-58661P 19970912 (60)
US 1997-55722P 19970818 (60)
US 1997-55723P 19970818 (60)
US 1997-55948P 19970818 (60)
US 1997-55949P 19970818 (60)
US 1997-55953P 19970818 (60)
US 1997-55950P 19970818 (60)
US 1997-55947P 19970818 (60)
US 1997-55964P 19970818 (60)
US 1997-55960P 19970818 (60)
US 1997-55684P 19970818 (60)
US 1997-55984P 19970818 (60)
US 1997-55954P 19970818 (60)
US 1997-51926P 19970708 (60)
US 1997-52793P 19970708 (60)
US 1997-51925P 19970708 (60)
US 1997-51928P 19970708 (60)
US 1997-52803P 19970708 (60)
US 1997-52732P 19970708 (60)
US 1997-51931P 19970708 (60)
US 1997-51932P 19970708 (60)
US 1997-51916P 19970708 (60)
US 1997-51930P 19970708 (60)
US 1997-51918P 19970708 (60)
US 1997-51920P 19970708 (60)
US 1997-52733P 19970708 (60)
US 1997-52795P 19970708 (60)
US 1997-51919P 19970708 (60)
US 1997-51928P 19970708 (60)
DT Utility
FS GRANTED
LN CNT 18742
INCL INCLM: 530/300.000
INCLM: 530/350.000; 435/069.100
NCLM: 530/300.000
NCLM: 530/350.000
NCLM: 435/069.100; 530/350.000

IC [7]
ICM: A61K038-00
ICS: C07K001-00; C12P021-06
530/300; 530/350; 435/69.1
EXP 530/300; 530/350; 435/69.1
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L18 ANSWER 22 OF 50 CAPLUS COPYRIGHT 2003 ACS
AN 2002.840857 CAPLUS
TI The cytoplasmic domain of the LDL receptor-related protein regulates
multiple steps in APP processing
AU Pierzick, Claus U.; Buesse, Tracy; Merriam, David E.; Weggen, Sascha; Koo,
Edward H.
CS Department of Neurosciences, University of California, San Diego, La
Jolla, CA, 92093 USA
SO EMBO Journal (2002), 21(21), 5691-5700
CODEN: EMODJG; ISSN: 0261-4189
PB Oxford University Press
DT Journal
LA English
RE CNT 44
THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
L18 ANSWER 23 OF 50 CAPLUS COPYRIGHT 2003 ACS
AN 2001.886449 CAPLUS
DN 136.36328
TI Alpha 2 macroglobulin receptors as
a heat shock protein receptor and uses thereof
IN Srivastava, Pramod K.
PA University of Connecticut Health Center, USA
SO PCT Int. Appl., 236 pp.
CODEN: PIXD2
DT Patent
LA English
FAN CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE
PI WO 2001092474 A1 20011206 WO 2001-US18041 20010604
W: AU, CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, TR
PRAI US 2000-20905P P 20000602
US 2000-625137 A 20000725
US 2000-668724 A 20000922
US 2000-750972 A 20001228
RE CNT 1
THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
L18 ANSWER 24 OF 50 CAPLUS COPYRIGHT 2003 ACS
AN 2001.763235 CAPLUS
DN 135.314399
TI Detection of variations in the DNA methylation profile of genes in the
determining the risk of disease
IN Berlin, Kurt; Piepenbrock, Christian; Olek, Alexander
PA Biogenomics A.-G., Germany
SO PCT Int. Appl., 636 pp.
CODEN: PIXD2
DT Patent
LA German
FAN CNT 68
PATENT NO. KIND DATE APPLICATION NO. DATE
PI WO 2001077373 A2 20011018 WO 2001-DE1486 20010406
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BY, BZ, CA, CH, CN,
CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,

RLI Continuation-in-part of Ser. No. US 1994-344836, filed on 23 Nov 1994, now abandoned Continuation-in-part of Ser. No. WO 1994-SE483, filed on 24 May 1994

PRAI SE 1993-1764 19930524

DT Utility

FS Granted

LN CNT 1058

INCL INCLM: 536/024.300

NCL INCLM: 514/044.000; 536/024.100

NCLM: 536/024.300

NCLM: 536/024.100

IC [7]

ICM: A61K031-7105

ICS: A61K031-711; C07H021-04

514/44; 536/24.1; 536/24.3

EXF INDEXING IS AVAILABLE FOR THIS PATENT.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 29 OF 50 USPTATFULT

AN 2001:79131 USPTATFULT

TI Family of protease inhibitors, and other biologic active substances

IN Voerman, Gerard, Brassaach, Belgium

PA Clodica, S.A., Luxembourg, Luxembourg (non-U.S. corporation)

PI US 6239106 B1 20010529

WO 9613585 19960509

US 1998-836686

WO 1995-EP4223

AI 19980327 (8)

19951027

19980327 PCT 371 date

19980327 PCT 102(e) date

PRAI EP 1994-117053 19941028

EP 1995-103637 19950314

DT Utility

FS Granted

LN CNT 813

INCL INCLM: 514/013.000

INCLM: 435/212.000; 435/213.000; 435/214.000; 435/215.000; 435/216.000;

435/217.000; 435/218.000; 435/219.000; 435/069.100; 435/252.300;

435/320.100; 536/023.200; 530/324.000; 530/350.000

NCLM: 514/013.000

NCLM: 435/069.100; 435/212.000; 435/213.000; 435/214.000; 435/215.000;

435/216.000; 435/217.000; 435/218.000; 435/219.000; 435/252.300;

435/320.100; 530/324.000; 530/350.000; 536/023.200

IC [7]

ICM: A61K038-00

ICS: C12N009-48; C12N001-20; C07H021-04

514/13; 435/212-219; 435/69.1; 435/252.3; 435/320.1; 536/23.2; 530/324;

530/350

EXF INDEXING IS AVAILABLE FOR THIS PATENT.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 30 OF 50 USPTATFULT

AN 2001:67794 USPTATFULT

TI Human respiratory syncytial virus peptides with anti-neurogenic and antiviral activities

IN Barney, Shawn O'lin, Cary, NC, United States

Lambert, Dennis Michael, Cary, NC, United States

Pettey, Stephen Robert, Cary, NC, United States

Trimeris, Inc., Durham, NC, United States (U.S. corporation)

PI US 6239983 B1 20010508

US 1995-485264 19950607 (8)

Division of Ser. No. US 1995-470896, filed on 6 Jun 1995

Continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994

Continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994

Continuation-in-part of Ser. No. US 1993-73028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933

DT Utility

FS Granted

LN CNT 32166

INCL INCLM: 530/300.000

NCL INCLM: 530/324.000; 530/325.000; 530/326.000; 424/211.100; 424/186.100

NCLM: 530/300.000

NCLM: 424/186.100; 424/211.100; 530/324.000; 530/325.000; 530/326.000

IC [7]

ICM: A61K038-00

ICS: 530/350; 530/324-329; 530/300; 424/211.1

EXF INDEXING IS AVAILABLE FOR THIS PATENT.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 31 OF 50 USPTATFULT

AN 2001:63243 USPTATFULT

TI Suppression of inhibitors

IN Brunner, Nils, Hellerup, Denmark

R.O. slashed.met, John, Copenhagen, Denmark

Ellis, Vincent, Woodford Green, United Kingdom

Pyke, Charles, Hiller.o slashed.d, Denmark

Gr.o slashed.ndahl-Hansen, Jan, Holte, Denmark

Pedersen, Helle, Aller.o slashed.d, Denmark

Hansen, Heine H.o slashed.i, Holte, Denmark

Dan.o slasheded. , Keld, Charlottelund, Denmark

PA Cancerforskningsfonden AF 1989, Copenhagen K, Denmark (non-U.S. corporation)

PI US 6224865 B1 20010501

US 9502413 19950126

WO 1996-583129 19960515 (8)

WO 1994-DK288 19940718

19960515 PCT 371 date

19960515 PCT 102(e) date

PRAI DK 1993-851 19930716

DT Utility

FS Granted

LN CNT 2471

INCL INCLM: 424/130.100

INCLM: 421/138.100; 421/141.100; 421/145.100; 421/155.100; 421/152.100;

421/158.100; 421/172.100; 421/179.100; 421/181.100; 421/183.100;

514/002.000

NCLM: 424/130.100

NCLM: 424/138.100; 424/141.100; 424/145.100; 424/152.100; 424/155.100;

424/158.100; 424/172.100; 424/179.100; 424/181.100; 424/183.100;

514/002.000

IC [7]

ICM: A61K039-395

ICS: A01N037-18

424/152.1; 424/141.1; 424/145.1; 424/155.1; 424/130.1; 424/138.1;

424/158.1; 424/172.1; 424/179.1; 424/181.1; 424/183.1; 514/2

EXF INDEXING IS AVAILABLE FOR THIS PATENT.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 32 OF 50 CAPLUS COPYRIGHT 2003 ACS

AN 2001:708596 CAPLUS

DN 136116223

TI Apolipoprotein E and apolipoprotein E receptors modulate

A.beta.-induced glial neuroinflammatory responses

AU Iadu, M. J.; Shah, J. A.; Reardon, C. A.; Getz, G. S.; Bu, G.; Hu, J.;

Guo, L.; Van Eldik, L. J.

CS Department of Medicine, Evanston Northwestern Healthcare Research

Institute, Evanston, IL, 60201, USA

SO Neurochemistry International (2001), 39(5-6), 427-434

CODEN: NEUROIS; ISSN: 0197-0186

PB Elsevier Science Ltd.

DT Journal; General Review

LA English

RE CNT 61

THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 33 OF 50 USPATFULT.
 AN 2000:102422 USPATFULT.
 TI Parasitic helminth p22 nucleic acid molecules
 Frank, Cynthia Ann, Ft. Collins, CO, United States
 Griewe, Robert B., Ft. Collins, CO, United States
 Heska Corporation, Ft. Collins, CO, United States
 Colorado State University Research Foundation, Ft. Collins, CO, United States (U.S. corporation)
 PI US 6100390
 US 1995-458860
 Continuation of Ser. No. US 1993-109391, filed on 19 Aug 1993, now patented, Pat. No. US 5639876 which is a continuation of Ser. No. US 1993-3357, filed on 12 Jan 1993, now abandoned Ser. No. Ser. No. US 1993-3389, filed on 12 Jan 1993, and Ser. No. US 1991-654226, filed on 12 Feb 1991, said Ser. No. US 3257 And Ser. No. US 3389 which is a continuation-in-part of Ser. No. US 654226
 DT Utility
 FS Granted
 LN.CNT 2469
 INCL INCLM: 536/023.700
 INCLS: 435/069.100; 435/069.300; 435/071.100; 536/022.100; 536/023.100; 536/024.320
 NCLM: 536/023.700
 NCLM: 536/023.700
 NCLM: 435/069.100; 435/069.300; 435/071.100; 536/022.100; 536/023.100; 536/024.320
 IC [7]
 ICM: C07H021-04
 ICS: C07H021-02; C12P021-06; C12P071-04
 536/22.1; 536/24.32; 536/23.1; 536/23.7; 435/69.1; 435/69.3; 435/71.1
 EXF INDEXING IS AVAILABLE FOR THIS PATENT.
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 L18 ANSWER 34 OF 50 USPATFULT.
 AN 2000:102109 USPATFULT.
 TI O-fucosyltransferase
 Wang, Yang, Milbrae, CA, United States
 Spellman, Michael W., Belmont, CA, United States (U.S. corporation)
 PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)
 PI US 6100076
 US 1997-978741
 Continuation-in-part of Ser. No. US 1997-792498, filed on 31 Jan 1997, now abandoned
 DT Utility
 FS Granted
 LN.CNT 3438
 INCL INCLM: 435/193.000
 NCLM: 435/193.000
 IC [7]
 ICM: C12N009-10
 EXP 435/193
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 L18 ANSWER 35 OF 50 USPATFULT.
 AN 2000:95093 USPATFULT.
 TI Isolated peptides derived from the Epstein-Barr virus
 Barney, Shawn O'Lin, Cary, NC, United States
 Lambert, Dennis Michael, Cary, NC, United States
 Petreway, Stephen Robert, Cary, NC, United States
 Trimeris, Inc., Durham, NC, United States (U.S. corporation)
 PA Trimeris, Inc., Durham, NC, United States (U.S. corporation)
 PI US 6093794
 US 1995-471913
 Division of Ser. No. US 1995-470896, filed on 6 Jun 1995 which is a continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994

which is a continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994 which is a continuation-in-part of Ser. No. US 1993-73028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933
 DT Utility
 FS Granted
 LN.CNT 19949
 INCL INCLM: 530/300.000
 INCLS: 530/324.000; 530/325.000; 530/326.000; 530/350.000; 424/186.100; 424/230.100
 NCLM: 530/300.000
 NCLM: 424/186.100; 424/230.100; 530/324.000; 530/325.000; 530/326.000; 530/350.000
 IC [7]
 ICM: A61K038-00
 ICS: A61K039-12; A61K039-245
 530/324; 530/388.3; 530/388.85; 530/389.4; 435/5; 424/147.1; 424/230.1
 EXF INDEXING IS AVAILABLE FOR THIS PATENT.
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 L18 ANSWER 36 OF 50 USPATFULT.
 AN 2000:67564 USPATFULT.
 TI Methods for inhibition of membrane fusion-associated events, including influenza virus
 Barney, Shawn O'Lin, Cary, NC, United States
 Lambert, Dennis Michael, Cary, NC, United States
 Petreway, Stephen Robert, Cary, NC, United States
 Trimeris, Inc., Durham, NC, United States (U.S. corporation)
 PA Trimeris, Inc., Durham, NC, United States (U.S. corporation)
 PI US 6068973
 US 1995-485551
 Division of Ser. No. US 1995-470896, filed on 6 Jun 1995 which is a continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994 which is a continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994 which is a continuation-in-part of Ser. No. US 1993-73028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933
 DT Utility
 FS Granted
 LN.CNT 12021
 INCL INCLM: 435/005.000
 INCLS: 530/324.000; 530/389.400; 424/147.100; 424/230.100; 424/206.100
 NCLM: 435/005.000
 NCLM: 424/147.100; 424/206.100; 424/230.100; 530/324.000; 530/389.400
 IC [7]
 ICM: C12Q001-70
 ICS: A61K038-00; A61K039-42; C07K016-00
 530/324; 530/389.4; 435/5; 424/147.1; 424/230.1; 424/206.1
 EXF INDEXING IS AVAILABLE FOR THIS PATENT.
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 L18 ANSWER 37 OF 50 USPATFULT.
 AN 2000:57361 USPATFULT.
 TI Compositions for inhibition of membrane fusion-associated events, including influenza virus transmission
 Barney, Shawn O'Lin, Cary, NC, United States
 Lambert, Dennis Michael, Cary, NC, United States
 Petreway, Stephen Robert, Cary, NC, United States
 Trimeris, Inc., Durham, NC, United States (U.S. corporation)
 PA Duke University, Durham, NC, United States (U.S. corporation)
 PI US 606065
 US 1995-475668
 Division of Ser. No. US 1995-470896, filed on 6 Jun 1995 which is a continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994 which is a continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994 which is a continuation-in-part of Ser. No. US 1993-73028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933
 DT Utility
 FS Granted
 LN.CNT 19987

INCL INCLM: 424/209.100
INCLIS: 424/186.100; 424/192.100; 424/206.100; 530/300.000; 530/324.000;
530/325.000; 530/326.000; 530/327.000; 530/328.000; 530/329.000;
530/330.000
NCL NCLM: 424/209.100
NCLIS: 424/186.100; 424/192.100; 424/206.100; 530/300.000; 530/324.000;
530/325.000; 530/326.000; 530/327.000; 530/328.000; 530/329.000;
530/330.000
IC [7]
ICM: A61K039-145
ICS: A61K039-12; A61K039-00; A61K038-00
424/209.1; 424/186.1; 424/192.1; 424/206.1; 530/300; 530/324; 530/325;
530/326; 530/327; 530/328; 530/329; 530/330
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L18 ANSWER 38 OF 50 USPATFULT
AN 2000:50515 USPATFULT
TI Screening assays for compounds that inhibit membrane fusion-associated
events
IN Barney, Shawn O'lin, Cary, NC, United States
Lambert, Dennis Michael, Cary, NC, United States
Peteway, Jr., Stephen Robert, Cary, NC, United States
Trimetris, Inc., Durham, NC, United States (U.S. corporation)
PA US 6054265 20000425
PI US 1997-919597 19970926 (8)
RLI Division of Ser. No. US 1995-470896, filed on 6 Jun 1995 which is a
continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994
which is a continuation-in-part of Ser. No. US 1994-255208, filed on 7
Jun 1994 which is a continuation-in-part of Ser. No. US 1993-73028,
filed on 7 Jun 1993, now patented, Pat. No. US 5464933
DT Utility
FS Granted
LN.CNT 21307
INCL INCLM: 435/005.000
INCLIS: 435/007.200
NCL NCLM: 435/005.000
NCLIS: 435/007.200
IC [7]
ICM: C120001-70
EXP 435/5; 435/7.2
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L18 ANSWER 39 OF 50 USPATFULT
AN 2000:12922 USPATFULT
TI Isolated peptides derived from human immunodeficiency virus
types 1 and 2 containing fusion inhibitory domains
IN Barney, Shawn O'lin, Cary, NC, United States
Lambert, Dennis Michael, Cary, NC, United States
Peteway, Jr., Stephen Robert, Cary, NC, United States
Trimetris, Inc., Durham, NC, United States (U.S. corporation)
PA US 6020459 20000201
PI US 1995-484223 19950607 (8)
RLI Division of Ser. No. US 1995-470896, filed on 6 Jun 1995 which is a
continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994
which is a continuation-in-part of Ser. No. US 1994-255208, filed on 7
Jun 1994 which is a continuation-in-part of Ser. No. US 1993-73028,
filed on 7 Jun 1993, now patented, Pat. No. US 5464933
DT Utility
FS Granted
LN.CNT 20335
INCL INCLM: 530/300.000
INCLIS: 530/324.000; 530/325.000; 530/326.000; 530/350.000; 424/188.100
NCL NCLM: 530/300.000
NCLIS: 530/324.000; 530/325.000; 530/326.000; 530/350.000; 424/188.100
IC [6]

ICM: A61K038-00
ICS: A61K039-21
530/300; 530/317; 530/324
EXP 530/300; 530/317; 530/324
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L18 ANSWER 40 OF 50 USPATFULT
AN 2000:9527 USPATFULT
TI Simian immunodeficiency virus peptides with antifusogenic and
antiviral activities
IN Barney, Shawn O'lin, Cary, NC, United States
Lambert, Dennis Michael, Cary, NC, United States
Peteway, Jr., Stephen Robert, Cary, NC, United States
Langlois, Inc., Durham, NC, United States
Trimetris, Inc., Durham, NC, United States (U.S. corporation)
PA US 6017536 20000125
PI US 1994-360107 19941220 (8)
RLI Continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994
which is a continuation-in-part of Ser. No. US 1993-73028, filed on 7
Jun 1993, now patented, Pat. No. US 5464933
DT Utility
FS Granted
LN.CNT 20227
INCL INCLM: 424/188.100
INCLIS: 424/208.100; 530/300.000; 530/324.000; 530/325.000; 530/326.000
NCL NCLM: 424/188.100
NCLIS: 424/208.100; 530/300.000; 530/324.000; 530/325.000; 530/326.000
IC [6]
ICM: A61K039-21
EXP 530/300; 530/324; 424/184.1; 424/188.1; 424/208.1
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L18 ANSWER 41 OF 50 USPATFULT
AN 2000:4427 USPATFULT
TI Measles virus peptides with antifusogenic and antiviral
activities
IN Barney, Shawn O'lin, Cary, NC, United States
Lambert, Dennis Michael, Cary, NC, United States
Peteway, Jr., Stephen Robert, Cary, NC, United States
Trimetris, Inc., Durham, NC, United States (U.S. corporation)
PA US 6013263 20000111
PI US 1995-486099 19950607 (8)
RLI Division of Ser. No. US 1995-470896, filed on 6 Jun 1995 which is a
continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994
Ser. No. Ser. No. US 1994-255208, filed on 7 Jun 1994 And Ser. No. US
1993-73028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933
DT Utility
FS Granted
LN.CNT 19827
INCL INCLM: 424/212.100
INCLIS: 530/300.000; 530/324.000; 530/325.000; 530/326.000; 424/184.100;
424/186.100
NCL NCLM: 424/212.100
NCLIS: 424/184.100; 424/186.100; 530/300.000; 530/324.000; 530/325.000;
530/326.000
IC [6]
ICM: A61K039-165
EXP 530/300; 530/324; 424/212.1
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L18 ANSWER 42 OF 50 CAPLUS COPYRIGHT 2003 ACS
AN 2000:185820 CAPLUS
DN 132:306738
TI Modulation of β -amyloid precursor protein processing by the
low density lipoprotein receptor-related protein (LRP). Evidence that LRP
contributes to the pathogenesis of Alzheimer's disease

No. US 1993-3257, filed on 12 Jan 1993, now abandoned Ser. No. Ser. No. US 1993-3389, filed on 12 Jan 1993, now abandoned And Ser. No. US 1991-654226, filed on 12 Feb 1991, now abandoned, said Ser. No. US 3257 which is a continuation-in-part of Ser. No. US 654226, said Ser. No. US 3389 which is a continuation-in-part of Ser. No. US 654226

Utility

DT Granted

FS Granted

LN CNT 2357

INCL INCLM: 536/023.700

NCL INCLM: 536/023.700

NCLM: 536/023.700

NCLM: 424/184.100; 424/185.100; 424/265.100; 435/007.220; 530/350.000;

IC [6]

ICM: C07H021-04

ICS: A61K039-00

EXF 424/184.1; 424/185.1; 424/265.1; 530/350; 530/300; 550/380; 550/387.1;

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 48 OF 50 USPTFUL

AN 97:104113 USPTFUL

TI Parastatic helminth p4 proteins

IN Tripp, Cynthia Ann, Ft. Collins, CO, United States

PA Frank, Glenn Robert, Ft. Collins, CO, United States

PA Griewe, Robert B., Ft. Collins, CO, United States

PA Heeka Corporation, Ft. Collins, CO, United States

PA Colorado State University Research Foundation, Ft. Collins, CO, United States (U.S. corporation)

PI US 5686080

AI US 1995-459019

RLI 19950602 (8)

Continuation of Ser. No. US 1993-109391, filed on 19 Aug 1993, now patented, Pat. No. US 5639876 which is a continuation-in-part of Ser. No. US 1993-3257, filed on 12 Jan 1993, now abandoned Ser. No. Ser. No. US 1993-3389, filed on 12 Jan 1993, now abandoned And Ser. No. US 1991-654226, filed on 12 Feb 1991, now abandoned, said Ser. No. US -3257 And Ser. No. US -3389, each Ser. No. US - which is a continuation-in-part of Ser. No. US -654226

DT Utility

FS Granted

LN CNT 2279

INCL INCLM: 424/265.100

NCL INCLM: 424/154.100; 424/185.100; 424/266.100; 530/350.000; 435/069.100;

NCLM: 424/265.100

NCLM: 424/265.100

NCLM: 424/184.100; 424/185.100; 424/266.100; 435/069.100; 435/069.300;

IC [6]

ICM: A61K039-00

ICS: A61K039-002; A61K039-38; C07K014-00

EXF 530/350; 530/300; 424/265.1; 424/266.1; 424/184.1; 424/185.1; 435/69.1;

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 49 OF 50 USPTFUL

AN 97:52122 USPTFUL

TI Nucleic acid molecules encoding novel parasitic helminth proteins

IN Tripp, Cynthia Ann, Ft. Collins, CO, United States

PA Frank, Glenn Robert, Ft. Collins, CO, United States

PA Griewe, Robert B., Ft. Collins, CO, United States

PA Heeka Corporation, Ft. Collins, CO, United States

PA Colorado State University Research Foundation, Ft. Collins, CO, United States (U.S. corporation)

PI US 5639876

AI US 1993-109391

RLI Continuation-in-part of Ser. No. US 1993-3257, filed on 12 Jan 1993, now abandoned Ser. No. Ser. No. US 1993-3389, filed on 12 Jan 1993, now abandoned And Ser. No. US 1991-654226, filed on 12 Feb 1991, now abandoned, said Ser. No. US -3257 And Ser. No. US -3389, each Ser. No. US - which is a continuation-in-part of Ser. No. US -654226

DT Utility

FS Granted

LN CNT 2327

INCL INCLM: 536/023.700

NCL INCLM: 536/023.700

NCLM: 536/023.700

NCLM: 424/184.100; 424/185.100; 424/265.100; 424/266.100

IC [6]

ICM: C07H019-00

ICS: C07H021-04; C12P021-04; A61K039-00

EXF 536/27; 536/22.1; 536/23.1; 536/23.7; 424/265.1; 424/269.1; 424/184.1;

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 50 OF 50 MEDLINE

AN 94365030 MEDLINE

DN 94365030 Pubmed ID: 8083232

TI The 39-kDa receptor-associated protein regulates ligand binding by the very low density lipoprotein receptor.

AU Batley F D; Galvelis M B; Fitzgerald D J; Argaves W S; Chappel D A;

CS Strauss J F 3rd; Strickland D R

CS Holland Laboratory, Department of Biochemistry, American Red Cross, Rockville, Maryland 20855.

NC CM42581 (NIGMS)

NC HL49264 (NHLBI)

NC HL50787 (NHLBI)

SO JOURNAL OF BIOLOGICAL CHEMISTRY. (1994 Sep 16) 269 (37) 23268-73.

CT United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199410

ED Entered STN: 19941021

ED Last Updated on STN: 19941021

ED Entered Medline: 19941011

=>

=> d hi

(FILE 'HOME' ENTERED AT 15:25:49 ON 20 FEB 2003)

FILE 'MEDLINE, CANCERLIT, BIOSIS, CONFSCI, EMBASE, CAPLUS, USPTFUL'.

ENTERED AT 15:26:27 ON 20 FEB 2003

L1 72563 S HEAT (A) SHOCK (A) PROTEIN

L2 40 S I1 AND ALPHA (A) 2 (A) MACROGLOBULIN (A) RECEPTOR

L3 33 DUP REM L2 (7 DUPLICATES REMOVED)

L4 12721 S I1 AND ANTIBODY?

L5 21 S I4 AND L2

L6 19 DUP REM L5 (2 DUPLICATES REMOVED)

L7 1585 S ACONIST? AND L1

L8 4 S L7 AND L2

L9 8637 S I1 AND PEPTIDE?

L10 27 S L9 AND L2

L11 24 DUP REM L10 (3 DUPLICATES REMOVED)

L12 11 S L11 AND MODULATE?

L13 1624 S ALPHA (A) 2 (A) MACROGLOBULIN (A) RECEPTOR
 L14 160 S L13 AND MODULAT?
 L15 110 DUP REM L14 (50 DUPLICATES REMOVED)
 L16 14 S L15 AND HEAT (A) SHOCK (A) PROTEIN
 L17 50 S L14 AND PEPTID?
 L18 50 DUP REM L17 (0 DUPLICATES REMOVED)
 => S L14 and antibody?
 L19 71 L14 AND ANTIBOD?
 => dup rem L19
 PROCESSING COMPLETED FOR L19
 L20 60 DUP REM L19 (11 DUPLICATES REMOVED)
 => d 120 not py=>2000
 'NOT' IS NOT A VALID FORMAT
 In a multifile environment, a format can only be used if it is valid
 in at least one of the files. Refer to file specific help messages
 or the STNGUIDE file for information on formats available in
 individual files.
 REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):exit
 'EXIT' IS NOT A VALID FORMAT
 In a multifile environment, a format can only be used if it is valid
 in at least one of the files. Refer to file specific help messages
 or the STNGUIDE file for information on formats available in
 individual files.
 REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):bye
 'BYE' IS NOT A VALID FORMAT
 In a multifile environment, a format can only be used if it is valid
 in at least one of the files. Refer to file specific help messages
 or the STNGUIDE file for information on formats available in
 individual files.
 REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):stop
 'STOP' IS NOT A VALID FORMAT
 In a multifile environment, a format can only be used if it is valid
 in at least one of the files. Refer to file specific help messages
 or the STNGUIDE file for information on formats available in
 individual files.
 REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):end
 => S 120 not py=>2000
 '2000' NOT A VALID FIELD CODE
 L21 13 L20 NOT PY=>2000
 => d 1-13
 L21 ANSWER 1 OF 13 MEDLINE
 AN 9715686 MEDLINE
 DN 9715686 Pubmed ID: 9003247
 TI Modulation of the alpha 2
 macroglobulin receptor/low density lipoprotein receptor
 related protein by interferon-gamma in human astroglial cells.
 AU Bushnaro R; Fabrizio C; Persichini T; Starace G; Ennas M G; Fumagalli L;
 Lauro G M
 CS Dipartimento di Scienze Cardiovascolari e Respiratorie, Universita La
 Sapienza, Rome, Italy.
 SO JOURNAL OF NEUROIMMUNOLOGY. (1997 Jan) 72 (1). 75-81.
 CY Journal code: 8109498. ISSN: 0165-5728.
 CY Netherlands
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 OS GENBANK-X55077
 EM 199702
 ED Entered STN: 19970305

Last Updated on STN: 19970305
 Entered Medline: 19970219
 L21 ANSWER 2 OF 13 MEDLINE
 AN 95072001 MEDLINE
 DN 95072001 Pubmed ID: 7526898
 TI Presence of LDL receptor-related protein/alpha 2-
 macroglobulin receptors in macrophages of
 atherosclerotic lesions from cholesterol-fed New Zealand and heterozygous
 Watanabe heritable hyperlipidemic rabbits.
 AU Daugherty A; Rateri D L
 CS Cardiovascular Division, Washington University School of Medicine, St.
 Louis, MO 63110.
 NC HT-17646 (NHLBI)
 SO ARTERIOSCLEROSIS AND THROMBOSIS. (1994 Dec) 14 (12) 2017-24.
 CY Journal code: 9101386. ISSN: 1049-8834.
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199412
 ED Entered STN: 19950116
 Last Updated on STN: 19960129
 Entered Medline: 19941230
 L21 ANSWER 3 OF 13 MEDLINE
 AN 9414468 MEDLINE
 DN 9414468 Pubmed ID: 7508685
 TI Expression of alpha 2-macroglobulin
 receptor/low density lipoprotein receptor-related protein and the
 39-kd receptor-associated protein in human trophoblasts.
 AU Coukos G; Gafvels M E; Wiesel S; Ruelaz E A; Strickland D K; Straus J F
 3rd; Coutifaris C
 CS Department of Obstetrics and Gynecology, University of Pennsylvania School
 of Medicine, Philadelphia.
 NC CM-42581 (NICMS)
 SO AMERICAN JOURNAL OF PATHOLOGY. (1994 Feb) 144 (2) 383-92.
 CY Journal code: 0370502. ISSN: 0002-9440.
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Abridged Index Medicus Journals; Priority Journals
 EM 199403
 ED Entered STN: 19940330
 Last Updated on STN: 19960129
 Entered Medline: 19940317
 L21 ANSWER 4 OF 13 MEDLINE
 AN 9236474 MEDLINE
 DN 9236474 Pubmed ID: 1502154
 TI Low density lipoprotein receptor-related protein/alpha 2
 macroglobulin receptor is an hepatic receptor for
 tissue-type plasminogen activator.
 AU By G; Williams S; Strickland D K; Schwartz A L
 CS Edward Mallinckrodt Department of Pediatrics, Washington University School
 of Medicine, St. Louis, MO 63110.
 NC H108467 (NHLBI)
 SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF
 AMERICA. (1992 Aug 15) 89 (16) 7427-31.
 CY Journal code: 7505876. ISSN: 0027-8424.
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English

FS Priority Journals
 ED 199209
 Entered STN: 19920925
 Last Updated on STN: 19980206
 Entered Medline: 19920915

L21 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2003 ACS
 AN 1999:180032 CAPLUS
 DN 13:11513
 TI Do p-glycoprotein and major vault protein (MVP/LMP) expression correlate with in vitro daunorubicin resistance in acute myeloid leukemia?
 AU Broxmeyer, H. J.; Sonnenfeld, P.; Peters, R.; Lankester, J.; Bekman, C. A.; Looijen, A. H.; Schuster, M.; Ossenkoppele, G. J.; Lowenberg, B.; Pinedo, H. M.; Schuurhuis, G. J.
 CS Department of Medical Oncology, University Hospital Vrije Universiteit, Amsterdam, 1007 MB, Neth.
 SO Leukemia (1999), 13(2), 258-265
 CODEN: LEUKED; ISSN: 0887-6624
 PB Stockton Press
 DT Journal
 LA English
 RE.CNT 34

THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2003 ACS
 AN 1997:188130 CAPLUS
 DN 126:275326
 TI Low density lipoprotein receptor-related protein modulates the expression of tissue-type plasminogen activator in human colon fibroblasts
 AU Hardy, Medora M.; Feder, Joseph; Wolfe, Richard A.; Bu, Guojun
 CS Dep. of Cell Culture and Biochemistry, Monsanto Co., St. Louis, MO, 63167, USA
 SO Journal of Biological Chemistry (1997), 272(10), 6812-6817
 CODEN: JBCHA3; ISSN: 0021-9258
 PB American Society for Biochemistry and Molecular Biology
 DT Journal
 LA English

L21 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2003 ACS
 AN 1997:82858 CAPLUS
 DN 126:169578
 TI The low-density lipoprotein receptor-related protein, a multifunctional apolipoprotein E receptor, modulates hippocampal neurite development
 AU Naita, Masaaki; Bu, Guojun; Holtzman, David M.; Schwartz, Alan L.
 CS Department of Pediatrics, Washington University School of Medicine, St. Louis, MO 63110, USA
 SO Journal of Neurochemistry (1997), 68(2), 567-595
 CODEN: JONRA9; ISSN: 0022-3042
 PB Lippincott-Raven
 DT Journal
 LA English

L21 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2003 ACS
 AN 1996:717281 CAPLUS
 DN 126:29495
 TI Apolipoprotein E-containing high density lipoprotein promotes neurite outgrowth and is a ligand for the low density lipoprotein receptor-related protein
 AU Fagan, Anne M.; Bu, Guojun; Sun, Yuling; Daugherty, Alan; Holtzman, David M.
 CS Dep. Neurology, Washington Univ. School Medicine, St. Louis, MO, 63110, USA
 SO Journal of Biological Chemistry (1996), 271(47), 30121-30125
 CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology
 DT Journal
 LA English

L21 ANSWER 9 OF 13 USPTFUL
 AN 1999:141305 USPTFUL
 TI Adjuvant for transcutaneous immunization
 AU Glenn, Gregory M.; Bethesda, MD, United States
 IN Alving, Carl R.; Bethesda, MD, United States
 PA The United States of America as represented by the U.S. Army Medical Research & Materiel Command, Washington, DC, United States (U.S. government)
 PI US 5980898
 AI US 1997-896085
 RLI Continuation-in-part of Ser. No. US 1996-749164, filed on 14 Nov 1996
 DT Utility
 FS Granted
 IN.CNT 198
 INCL INCLM: 424/184.100
 INCLS: 424/449.000; 424/450.000; 424/236.000; 424/240.100; 424/241.100; 424/275.100; 530/363.000; 530/403.000
 NCLM: 424/184.100
 NCLS: 424/085.100; 424/240.100; 424/241.100; 424/275.100; 424/449.000; 424/450.000; 530/363.000; 530/403.000

IC [6]
 ICS: A61K039-00
 EXF 424/449; 424/450; 424/184.1; 424/236; 424/240.1; 424/241.1; 424/275.1; 530/363; 530/403
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L21 ANSWER 10 OF 13 USPTFUL
 AN 1999:67356 USPTFUL
 TI Parasitic helminth p220 proteins
 AU Tripp, Cynthia Ann, Ft. Collins, CO, United States
 IN Frank, Glenn Robert, Ft. Collins, CO, United States
 PA Heesla Corporation, Ft. Collins, CO, United States (U.S. corporation)
 PI US 5912337
 AI US 1995-460428
 RLI Continuation of Ser. No. US 1993-109391, filed on 19 Aug 1993, now patented, Pat. No. US 5639876 which is a continuation-in-part of Ser. No. US 1993-3257, filed on 12 Jan 1993, now abandoned Ser. No. US 1991-654226, filed on 12 Feb 1991, now abandoned, said Ser. No. US 1991-654226, which is a continuation-in-part of Ser. No. US 654226 3389 which is a continuation-in-part of Ser. No. US 654226
 DT Utility
 FS Granted
 IN.CNT 2357
 INCL INCLM: 536/023.700
 INCLS: 424/184.100; 424/185.100; 424/265.100; 530/350.000; 550/387.100
 NCLM: 536/023.700
 NCLS: 424/184.100; 424/185.100; 424/265.100; 435/007.220; 530/350.000; 530/387.100

IC [6]
 ICS: C07H021-04
 EXF 424/184.1; 424/185.1; 424/265.1; 530/350; 530/380; 550/387.1; 550/388.2; 536/23.7
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L21 ANSWER 11 OF 13 USPTFUL

AN 1998:30893 USPTAFULL
 TI Non-mammalian DNA virus to express an exogenous gene in a mammalian cell
 IN Boyce, Frederick M., Belmont, MA, United States
 PA The General Hospital Corporation, Boston, MA, United States (U.S. corporation)
 PI US 5731182 19980124
 RLI US 1995-486341 19950607 (8)
 DT Continuation-in-part of Ser. No. US 1994-311157, filed on 23 Sep 1994
 PS Utility
 INCL Granted
 LN.CNT 1730
 INCLM: 435/183.000
 INCLS: 435/320.100; 435/069.100; 435/070.100
 NCLM: 435/183.000
 NCLS: 435/069.100; 435/070.100; 435/320.100
 IC [6]
 ICM: C12N009-00
 ICS: C12N015-63; C12P021-02
 EXP 435/183; 435/183T; 435/320.1; 435/69.1; 435/70.1
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L21 ANSWER 12 OF 13 USPTAFULL
 AN 97:104113 USPTAFULL
 TI Parasitic helminth p4 proteins
 IN Tripp, Cynthia Ann, Ft. Collins, CO, United States
 PA Frank, Glenn Robert, Ft. Collins, CO, United States
 PI Heesla Corporation, Ft. Collins, CO, United States (U.S. corporation)
 RLI Colorado State University Research Foundation, Ft. Collins, CO, United States (U.S. corporation)
 AI US 5686080 19971111
 RLI US 1995-459019 19950602 (8)
 DT Continuation of Ser. No. US 1993-109391, filed on 19 Aug 1993, now patented, Pat. No. US 5639876 which is a continuation-in-part of Ser. No. US 1993-3389, filed on 12 Jan 1993, now abandoned and Ser. No. US 1991-654226, filed on 12 Feb 1991, now abandoned and Ser. No. US -3257 And Ser. No. US -3389, each Ser. No. US - which is a continuation-in-part of Ser. No. US -654226
 PS Utility
 INCL Granted
 LN.CNT 2279
 INCLM: 424/265.100
 INCLS: 424/154.100; 424/185.100; 424/266.100; 530/350.000; 435/069.100; 435/069.300; 435/071.100
 NCLM: 424/265.100
 NCLS: 424/184.100; 424/185.100; 424/266.100; 435/069.100; 435/069.300; 435/071.100; 530/350.000
 IC [6]
 ICM: A61K039-00
 ICS: A61K039-002; A61K039-38; C07K014-00
 EXP 530/350; 530/300; 424/265.1; 424/266.1; 424/184.1; 424/185.1; 435/69.1; 435/69.3; 435/71.1
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L21 ANSWER 13 OF 13 USPTAFULL
 AN 97:52122 USPTAFULL
 TI Nucleic acid molecules encoding novel parasitic helminth proteins
 IN Tripp, Cynthia Ann, Ft. Collins, CO, United States
 PA Frank, Glenn Robert, Ft. Collins, CO, United States
 PI Heesla Corporation, Ft. Collins, CO, United States (U.S. corporation)
 RLI Colorado State University Research Foundation, Ft. Collins, CO, United States (U.S. corporation)
 AI US 5639876 19970617

AI US 1993-109391 19930819 (8)
 RLI Continuation-in-part of Ser. No. US 1993-3257, filed on 12 Jan 1993, now abandoned and Ser. No. Ser. No. US 1993-3389, filed on 12 Jan 1993, now abandoned and Ser. No. US 1991-654226, filed on 12 Feb 1991, now abandoned and Ser. No. US -3257 And Ser. No. US -3389, each Ser. No. US - which is a continuation-in-part of Ser. No. US -654226
 DT Utility
 PS Granted
 INCL 2327
 INCLM: 536/023.700
 INCLS: 536/022.100; 536/023.100; 435/069.100; 435/069.300; 435/071.100; 424/184.100; 424/185.100; 424/265.100; 424/266.100
 NCLM: 536/023.700
 NCLS: 424/184.100; 424/185.100; 424/265.100; 424/266.100; 435/069.100; 435/069.300; 435/071.100; 536/022.100; 536/023.100
 IC [6]
 ICM: C07H019-00
 ICS: C07H021-04; C12P021-04; A61K039-00
 EXP 536/27; 536/22.1; 536/23.1; 536/23.7; 424/265.1; 424/269.1; 424/184.1; 424/185.1; 424/165.1; 424/266.1; 435/69.1; 435/69.3; 435/71.1
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d his
 (FILE 'HOME' ENTERED AT 15:25:49 ON 20 FEB 2003)
 FILE 'MEDLINE, CANCERLIT, BIOSIS, CONFSCI, EMBASE, CAPLUS, USPTAFULL' ENTERED AT 15:26:27 ON 20 FEB 2003
 L1 72563 S HEAT (A) SHOCK (A) PROTEIN
 L2 40 S L1 AND ALPHA (A) 2 (A) MACROGLOBULIN (A) RECEPTOR
 L3 33 DUP REM L2 (7 DUPLICATES REMOVED)
 L4 12721 S L1 AND ANTIBODY?
 L5 21 S L4 AND L2
 L6 19 DUP REM L5 (2 DUPLICATES REMOVED)
 L7 1585 S AGONIST? AND L1
 L8 4 S L7 AND L2
 L9 8637 S L1 AND PEPTIDE?
 L10 27 S L9 AND L2
 L11 24 DUP REM L10 (3 DUPLICATES REMOVED)
 L12 11 S L11 AND MODULATE?
 L13 1624 S ALPHA (A) 2 (A) MACROGLOBULIN (A) RECEPTOR
 L14 160 S L13 AND MODULATE?
 L15 110 DUP REM L14 (50 DUPLICATES REMOVED)
 L16 14 S L15 AND HEAT (A) SHOCK (A) PROTEIN
 L17 50 S L14 AND PEPTID?
 L18 50 DUP REM L17 (0 DUPLICATES REMOVED)
 L19 71 S L14 AND ANTIBODY?
 L20 60 DUP REM L19 (11 DUPLICATES REMOVED)
 L21 13 S L20 NOT PY=>2000

=> s l14 and tpa
 L22 7 l14 AND tpa
 => d l-7
 L22 ANSWER 1 OF 7 USPTAFULL
 AN 2003:37187 USPTAFULL
 TI Anticolic liposomes for delivery of bioactive agents
 IN Lakkaraju, Aparna, Minneapolis, MN, UNITED STATES
 PA Dubinsky, Janet M., St. Paul, MN, UNITED STATES
 PI Low, Walter, Shorewood, MN, UNITED STATES
 RLI Rahman, Yueh-Erh, LaJolla, CA, UNITED STATES
 AI US 2003026831 A1 20030206
 PI US 2002-131786 A1 20020422 (10)

PRAI US 2001-285337P 20010420 (60)
 DT Utility
 FS APPLICATION
 LN.CNT 3617
 INCL INCLM: 424/450.000
 NCL NCLM: 424/450.000
 IC [7]
 ICM: A61K009-127

 L22 ANSWER 2 OF 7 USPTAFULL
 AN 2003:10238 USPTAFULL
 TI Secreted protein HLHP03
 IN Fischer, Carrie L., Burke, VA, UNITED STATES
 Rosen, Craig A., Laytonville, MD, UNITED STATES
 Soppet, Daniel R., Centerville, VA, UNITED STATES
 Ruben, Steven M., Olney, MD, UNITED STATES
 Kyaw, Hla, Frederick, CA, UNITED STATES
 Li, Yi, Sunnyvale, CA, UNITED STATES
 Zeng, Zhizhen, Lansdale, PA, UNITED STATES
 Lafleur, David W., Washington, DC, UNITED STATES
 Moore, Paul A., Germantown, MD, UNITED STATES
 Shi, Yangu, Gaithersburg, MD, UNITED STATES
 Olsen, Henrik S., Gaithersburg, MD, UNITED STATES
 Ebner, Reinhard, Gaithersburg, MD, UNITED STATES
 Brewer, Laurie A., St. Paul, MN, UNITED STATES
 PI US 2001-983802 A1 20030130
 AI Continuation of Ser. No. US 1999-227357, filed on 8 Jan 1999, GRANTED,
 RLI Pat. No. US 6342581 Continuation-in-part of Ser. No. WO 1998-US13684,
 filed on 7 Jul 1998, UNKNOWN
 PRAI US 1997-51926P 19970708 (60)
 US 1997-52793P 19970708 (60)
 US 1997-51925P 19970708 (60)
 US 1997-51929P 19970708 (60)
 US 1997-52803P 19970708 (60)
 US 1997-52732P 19970708 (60)
 US 1997-51931P 19970708 (60)
 US 1997-51932P 19970708 (60)
 US 1997-51916P 19970708 (60)
 US 1997-51930P 19970708 (60)
 US 1997-51918P 19970708 (60)
 US 1997-51920P 19970708 (60)
 US 1997-52733P 19970708 (60)
 US 1997-52795P 19970708 (60)
 US 1997-51919P 19970708 (60)
 US 1997-51928P 19970708 (60)
 US 1997-55722P 19970818 (60)
 US 1997-55723P 19970818 (60)
 US 1997-55948P 19970818 (60)
 US 1997-55949P 19970818 (60)
 US 1997-55953P 19970818 (60)
 US 1997-55950P 19970818 (60)
 US 1997-55947P 19970818 (60)
 US 1997-55964P 19970818 (60)
 US 1997-56160P 19970818 (60)
 US 1997-55684P 19970818 (60)
 US 1997-55844P 19970818 (60)
 US 1997-55954P 19970912 (60)
 US 1997-58785P 19970912 (60)
 US 1997-58664P 19970912 (60)
 US 1997-58660P 19970912 (60)
 US 1997-58661P 19970912 (60)
 DT Utility
 FS APPLICATION
 LN.CNT 19390

INCL INCLM: 435/006.000
 INCLS: 435/069.100; 435/325.000; 435/320.100; 435/183.000; 536/023.200
 NCL NCLM: 435/006.000
 NCLS: 435/069.100; 435/325.000; 435/320.100; 435/183.000; 536/023.200
 IC [7]
 ICM: C12Q001-68
 ICS: C07H021-04; C12N009-00; C12P021-02; C12N005-06
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

 L22 ANSWER 3 OF 7 USPTAFULL
 AN 2002:19393 USPTAFULL
 TI Secreted protein HLHP03
 IN Rosen, Craig A., Laytonville, MD, United States
 Ruben, Steven M., Olney, MD, United States
 Olsen, Henrik S., Gaithersburg, MD, United States
 Ebner, Reinhard, Gaithersburg, MD, United States
 Human Genome Sciences, Inc., Rockville, MD, United States (U.S. corporation)
 PA
 PI US 6342581 B1 20020129
 AI US 1999-227357 19990108 (9)
 RLI Continuation-in-part of Ser. No. WO 1998-US13684, filed on 7 Jul 1998
 PRAI US 1997-58785P 19970912 (60)
 US 1997-58664P 19970912 (60)
 US 1997-58660P 19970912 (60)
 US 1997-58661P 19970912 (60)
 US 1997-58722P 19970818 (60)
 US 1997-55723P 19970818 (60)
 US 1997-55948P 19970818 (60)
 US 1997-55949P 19970818 (60)
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 US 1997-55947P 19970818 (60)
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 US 1997-55984P 19970818 (60)
 US 1997-55954P 19970818 (60)
 US 1997-51926P 19970708 (60)
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 US 1997-51925P 19970708 (60)
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 US 1997-52803P 19970708 (60)
 US 1997-52732P 19970708 (60)
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 US 1997-51932P 19970708 (60)
 US 1997-51916P 19970708 (60)
 US 1997-51930P 19970708 (60)
 US 1997-51918P 19970708 (60)
 US 1997-51920P 19970708 (60)
 US 1997-52733P 19970708 (60)
 US 1997-52795P 19970708 (60)
 US 1997-51919P 19970708 (60)
 US 1997-51928P 19970708 (60)
 DT Utility
 FS GRANTED
 LN.CNT 18742
 INCL INCLM: 530/300.000
 INCLS: 530/350.000; 435/069.100
 NCL NCLM: 530/300.000
 NCLS: 435/069.100; 530/350.000
 IC [7]
 ICM: A61K038-00
 ICS: C07K001-00; C12P021-06
 EXF 530/300; 530/350; 435/69.1
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L22 ANSWER 4 OF 7 USPTFULL
 AN 2001:18694 USPTFULL
 TI Suppression of inhibitors
 IN Brunner, Nils, Vitum, Denmark
 Komer, John, Copenhagen, Denmark
 Elise, Vincent, Woodford Green, Great Britain
 Pyke, Charles, Copenhagen, Denmark
 Grondahl-Hansen, Jan, Holte, Denmark
 Pappot, Helle Pedersen, Allerod, Denmark
 Hansen, Heine Hol, Holte, Denmark
 Dano, Keid, Charlottenlund, Denmark
 PI US 2001034327 AI 20010418 (9)
 AI US 2001-836323
 RLI Division of Ser. No. US 1996-583129, filed on 15 May 1996, GRANTED, Pat.
 No. US 6224865 A 371 of International Ser. No. WO 1994-DK288, filed on
 18 Jul 1994, UNKNOWN 19930716
 PRAI DK 1993-851
 DT Utility
 FS APPLICATION
 LN CNT 2247
 INCL INCLM: 514/012.000
 INCLM: 435/007.230
 NCLM: 514/012.000
 NCLM: 435/007.230
 IC [7]
 ICM: G01N033-574
 ICS: A61K038-55
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L22 ANSWER 5 OF 7 USPTFULL
 AN 2001:125760 USPTFULL
 TI O-fucosyltransferase
 IN Wang, Yang, Milbrase, CA, United States
 Spellman, Michael W., Belmont, CA, United States
 Genentech, Inc., South San Francisco, CA, United States (U.S.
 corporation)
 PI US 6270987 B1 20010807
 AI US 1999-333729 19990615 (9)
 RLI Division of Ser. No. US 1997-978741, filed on 26 Nov 1997, now patented,
 Pat. No. US 6100076, issued on 8 Aug 2000 Continuation-in-part of Ser.
 No. US 1997-792498, filed on 31 Jan 1997, now abandoned
 DT Utility
 FS GRANTED
 LN CNT 3080
 INCL INCLM: 435/068.100
 INCLM: 435/015.000; 435/053.000; 435/041.000; 435/072.000; 435/097.000;
 INCLM: 435/193.000; 435/200.000
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 NCLM: 435/015.000; 435/041.000; 435/053.000; 435/072.000; 435/097.000;
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 ICM: C12N009-00
 ICS: C12N009-10
 EXP 435/115.435/68.1.435/53.435/41.435/72.435/97.435/193.435/200
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L22 ANSWER 6 OF 7 USPTFULL
 AN 2001:63243 USPTFULL
 TI Suppression of inhibitors
 IN Brunner, Nils, Hellerup, Denmark
 R.O. slashed, mer, John, Copenhagen, Denmark
 Elise, Vincent, Woodford Green, United Kingdom
 Pyke, Charles, Hillerød, Denmark
 Gr.O. slashed, ndahl-Hansen, Jan, Holte, Denmark

PA Pedersen, Helle, Allerød slashed.d, Denmark
 Hansen, Heine H.O. slashed.i, Holte, Denmark
 Dano slashed, Keid, Charlottenlund, Denmark
 Cancerforskningsfonden AF 1989, Copenhagen K, Denmark (non-U.S.
 corporation)
 PI US 6224865 B1 20010501
 AI WO 9502413 19950126
 AI US 1996-583129 19960515 (8)
 WO 1994-DK288 19940718
 PRAI DK 1993-851 19960515 PCT 371 date
 DT Utility
 FS Granted
 LN CNT 2471
 INCL INCLM: 424/130.100
 INCLM: 421/138.100; 421/141.100; 421/145.100; 421/155.100; 421/152.100;
 INCLM: 421/158.100; 421/172.100; 421/179.100; 421/181.100; 421/183.100;
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 ICS: A01N037-18
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 424/158.1.424/172.1.424/179.1.424/181.1.424/183.1.514/2
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L22 ANSWER 7 OF 7 USPTFULL
 AN 2000:102109 USPTFULL
 TI O-fucosyltransferase
 IN Wang, Yang, Milbrase, CA, United States
 Spellman, Michael W., Belmont, CA, United States
 Genentech, Inc., South San Francisco, CA, United States (U.S.
 corporation)
 PI US 6100076 20000808
 AI US 1997-978741 19971126 (8)
 RLI Continuation-in-part of Ser. No. US 1997-792498, filed on 31 Jan 1997,
 now abandoned
 DT Utility
 FS Granted
 LN CNT 3438
 INCL INCLM: 435/193.000
 NCLM: 435/193.000
 IC [7]
 ICM: C12N009-10
 ICS: 435/193
 EXP 435/193
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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 L2 40 S L1 AND ALPHA (A) 2 (A) MACROGLOBULIN (A) RECEPTOR
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 L4 12721 S L1 AND ANTIBODY
 L5 21 S L4 AND L2
 L6 19 DUP REM L5 (2 DUPLICATES REMOVED)
 L7 1585 S ACONIST? AND L1

L8 4 S L7 AND L2
L9 8637 S L1 AND PEPTIDE?
L10 27 S L1 AND L2
L11 24 DUP REM L10 (3 DUPLICATES REMOVED)
L12 11 S L11 AND MODULATE?
L13 1624 S ALPHA (A) 2 (A) MACROGLOBULIN (A) RECEPTOR
L14 160 S L13 AND MODULATE?
L15 110 DUP REM L14 (50 DUPLICATES REMOVED)
L16 14 S L15 AND HEAT (A) SHOCK (A) PROTEIN
L17 50 S L14 AND PEPTID?
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L19 71 S L14 AND ANTIBOD?
L20 60 DUP REM L19 (11 DUPLICATES REMOVED)
L21 13 S L20 NOT PY->2000
L22 7 S L14 AND TPA

=> 8 L14 and tissue (a) type (a) plasminogen (a) activator
L23 11 L14 AND TISSUE (A) TYPE (A) PLASMINOGEN (A) ACTIVATOR

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PROCESSING COMPLETED FOR L23
L24 7 DUP REM L23 (4 DUPLICATES REMOVED)

=> d 1-7

L24 ANSWER 1 OF 7 USPATFULL
AN 2003:37603 USPATFULL
TI Human CDNA's and proteins and uses thereof
IN Tanaka, Hiroaki, Antony, FRANCE
PA GENSET, S.A., Paris, FRANCE, 75008 (non-U.S. corporation)
PI US 2001-924340 A1 20030206
AI US 2001-305456P A1 20010713 (60)
PRAI US 2001-302277P 20010629 (60)
US 2001-298698P 20010615 (60)
US 2001-293574P 20010525 (60)

DT Utility
FS APPLICATION
LN CNT 25650
INCL INCLM: 435/069.100
INCLM: 435/183.000; 435/320.100; 435/325.000; 530/350.000; 536/023.200;
NCLM: 435/069.100
NCLM: 435/183.000; 435/320.100; 435/325.000; 530/350.000; 536/023.200;
NCLM: 435/069.100

IC [7]
ICM: C12P021-02
ICS: C120001-68; C07H021-04; C12N009-00; C12N005-06

L24 ANSWER 2 OF 7 USPATFULL
AN 2003:37516 USPATFULL
TI Human CDNA's and proteins and uses thereof
IN Bejani, Stephane, Paris, FRANCE
PA Tanaka, Hiroaki, Antony, FRANCE
PI GENSET, S.A., Paris, FRANCE, 75008 (non-U.S. corporation)
PI US 2003027161 A1 20030206
AI US 2001-992600 A1 20011113 (9)
R1 Division of Ser. No. US 2001-924340, filed on 6 Aug 2001, PENDING
PRAI WO 2001-181715 20010806
US 2001-305456P 20010713 (60)
US 2001-302277P 20010629 (60)
US 2001-298698P 20010615 (60)
US 2001-293574P 20010525 (60)

DT Utility

FS APPLICATION
LN CNT 25529
INCL INCLM: 435/006.000
INCLM: 435/069.100; 435/183.000; 435/320.100; 435/325.000; 530/350.000;
NCLM: 435/069.100; 800/008.000
NCLM: 435/006.000
NCLM: 435/069.100; 435/183.000; 435/320.100; 435/325.000; 530/350.000;
NCLM: 435/023.200; 800/008.000

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ICM: C120001-68
ICS: A01K067-00; C07H021-04; C12N009-00; C12P021-02; C12N005-06

L24 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2003 ACS
AN 2001:886449 CAPLUS
DN 136:36328
TI Alpha 2 macroglobulin receptors as
IN a heat shock protein receptor and uses thereof
IN Stivastava, Pramod K.
PA University of Connecticut Health Center, USA
SO PCT Int. Appl., 236 pp.
DT Patent
LA English
FAN CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE
P1 WO 2001092474 A1 20011206 WO 2001-US18041 20010604
W: AU, CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, TR
PRAI US 2000-209095P P 20000602
US 2000-625137 A 20000725
US 2000-668724 A 20000922
US 2000-750972 A 20001228
RE CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

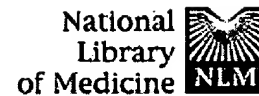
L24 ANSWER 4 OF 7 USPATFULL
AN 2001:188694 USPATFULL
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IN Romer, John, Copenhagen, Denmark
IN Ellis, Vincent, Woodford Green, Great Britain
IN Pyke, Charles, Copenhagen, Denmark
IN Grondahl-Hansen, Jan, Holte, Denmark
IN Pappot, Heine Pedersen, Allerod, Denmark
IN Hansen, Heine Hol, Holte, Denmark
IN Danu, Keld, Charlottenlund, Denmark
PI US 2001034327 A1 20011025
AI US 2001-836323 A1 20010418 (9)
R1 Division of Ser. No. US 1996-583129, filed on 15 May 1996, GRANTED, Pat.
PRAI No. US 6224865 A 371 of International Ser. No. WO 1994-DK288, filed on
18 Jul 1994, UNKNOWN
DK 1993-851 19930716

DT Utility
FS APPLICATION
LN CNT 2247
INCL INCLM: 514/012.000
INCLM: 435/007.230
NCLM: 514/012.000
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IC [7]
ICM: G01N033-574
ICS: A61K038-55

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L24 ANSWER 5 OF 7 USPATFULL
 AN 2001:63243 USPATFULL
 TI Suppression of inhibitors
 IN Brunner, Nils, Hellerup, Denmark
 R.O. slashed mer. John, Copenhagen, Denmark
 Ellis, Vincent, Woodford Green, United Kingdom
 Pyke, Charles, Hillerød slashed.d, Denmark
 Gr.O slashed.ndahl-Hansen, Jan, Hølte, Denmark
 Pedersen, Helle, Allerød slashed.d, Denmark
 Hansen, Heine H.O slashed.i, Hølte, Denmark
 Dan.O slashed. , Keld, Charlottenlund, Denmark
 Cancerforskningsfonden AF 1989, Copenhagen K, Denmark (non-U.S. corporation)
 PA US 6224865 B1 20010501
 PI WO 9502413 19950126
 AI US 1996-583129 19960515 (8)
 WO 1994-DK288 19940718
 19960515 PCT 371 date
 19960515 PCT 102(e) date
 19930716
 PRAI DK 1993-851
 DT Utility
 FS Granted
 LN.CNT 2471
 INCL INCLM: 424/130.100
 INCLS: 421/138.100; 421/141.100; 421/145.100; 421/155.100; 421/152.100;
 421/158.100; 421/172.100; 421/179.100; 421/181.100; 421/183.100;
 514/002.000
 NCLM: 424/130.100
 NCLS: 424/138.100; 424/141.100; 424/145.100; 424/152.100; 424/155.100;
 424/158.100; 424/172.100; 424/179.100; 424/181.100; 424/183.100;
 514/002.000
 IC [7]
 ICM: A61K039-395
 ICS: A01N037-18
 EXF 424/152.1: 424/141.1; 424/145.1; 424/155.1; 424/130.1; 424/138.1;
 424/158.1; 424/172.1; 424/179.1; 424/181.1; 424/183.1; 514/2
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 L24 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2003 ACS
 AN 1997:188130 CAPLUS
 DN 126:275326
 TI Low density lipoprotein receptor-related protein modulates the
 expression of tissue-type plasminogen
 activator in human colon fibroblasts
 AU Hardy, Medora M.; Feder, Joseph; Wolfe, Richard A.; Bu, Guojun
 CS Dep. of Cell Culture and Biochemistry, Monsanto Co., St. Louis, MO. 63167,
 USA
 SO Journal of Biological Chemistry (1997), 272(10), 6812-6817
 CODEN: JBCHA3; ISSN: 0021-9258
 PB American Society for Biochemistry and Molecular Biology
 DT Journal
 LA English
 L24 ANSWER 7 OF 7 MEDLINE
 AN 92366474 MEDLINE
 DN 92366474 PubMed ID: 1502154
 TI Low density lipoprotein receptor-related protein/alpha 2
 -macroglobulin receptor is an hepatic receptor for
 tissue-type plasminogen activator.
 BU G; Williams S; Strickland D K; Schwartz A L
 CS Edward Mallinckrodt Department of Pediatrics, Washington University School
 of Medicine, St. Louis, MO 63110.
 NC HL08467 (NHLBI)
 HL17646 (NHLBI)

SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF
 AMERICA, (1992 Aug 15) 89 (16) 7427-31.
 Journal code: 7505876. ISSN: 0027-8424.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199209
 ED Entered STN: 19920925
 Last Updated on STN: 19980206
 Entered Medline: 19920915
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☐ 1: Exp Cell Res 1999 Sep 15;251(2):433-41

Related Articles, Links

ELSEVIER SCIENCE
FULL-TEXT ARTICLE

Characterization of the soluble form of the low density lipoprotein receptor-related protein (LRP).

Quinn KA, Pye VJ, Dai YP, Chesterman CN, Owensby DA.

Centre for Thrombosis and Vascular Research, School of Pathology,
Kensington, New South Wales, 2052, Australia. k.quinn@unsw.edu.au

We report characterization of the soluble form of the low density lipoprotein receptor-related protein (sLRP) which circulates in human plasma. Amino acid sequence analysis confirmed that sLRP isolated from human plasma contains the alpha-chain of LRP1. In addition, Western blot analysis identified a truncated beta-chain noncovalently associated with the purified alpha-chain. The molecular size (M(r) 55K) of the peptide portion of the truncated beta-chain indicates that the subunit comprises the extracellular portion of the beta-chain and terminates in a membrane-proximal region. We investigated the mechanism by which sLRP may be generated using the trophoblast cell line, BeWo, which releases sLRP in culture. Cell surface labeling experiments indicate that LRP is released from BeWo cells following expression at the cell surface. Incubation of BeWo cells in the presence of a metalloproteinase inhibitor, INH-3855-PI, results in a dose-dependent inhibition of LRP shedding. The metalloproteinase responsible for the shedding of LRP by BeWo cells is not up-regulated by phorbol ester and is not dependent on serine proteases, such as plasmin, for activity. The BeWo cell line is derived from a human gestational choriocarcinoma and preliminary studies suggest that LRP may be shed within the placenta during gestation. Increased levels of sLRP were detected in cord blood. In term placenta, LRP is expressed in the syncytium, which comprises the maternal-fetal interface. Increased levels of sLRP in cord blood may reflect cellular dysfunction and increased metalloproteinase activity at this important interface. Copyright 1999 Academic Press.

PMID: 10471328 [PubMed - indexed for MEDLINE]

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☐ 1: Circulation 1997 Jan 7;95(1):46-52

Related Articles, Links

**FREE full text article at
circ.ahajournals.org****Antagonists of the mannose receptor and the LDL receptor-related protein dramatically delay the clearance of tissue plasminogen activator.****Biessen EA, van Teijlingen M, Vietsch H, Barrett-Bergshoeff MM, Bijsterbosch MK, Rijken DC, van Berkel TJ, Kuiper J.**

Division of Biopharmaceutics, Leiden/Amsterdam Center for Drug Research, University of Leiden, The Netherlands.

BACKGROUND: Clinical application of tissue plasminogen activator (TPA) as a fibrinolytic agent is complicated by its rapid clearance from the bloodstream, which is caused by TPA liver uptake. The mannose receptor on endothelial liver cells and the LDL receptor-related protein (LRP) on parenchymal liver cells were reported to contribute to liver uptake. **METHODS AND RESULTS:** In this study, we addressed whether TPA clearance can be delayed by inhibiting receptor-mediated endocytosis of TPA. A series of cluster mannosides was synthesized, and their affinity for the mannose receptor was determined. A cluster mannoside carrying six mannose groups (M6L5) displayed a subnanomolar affinity for the mannose receptor ($K_i = 0.41 \pm 0.09$ nmol/L). Preinjection of M6L5 (1.2 mg/kg) reduced the clearance of ^{125}I -TPA in rats by 60% because of specific inhibition of the endothelial cell uptake. The low toxicity of M6L5, combined with its accessible synthesis and high specificity for the mannose receptor, makes it a promising agent to improve the pharmacokinetics of TPA. Blockade of LRP by 39-kD receptor-associated protein (GST-RAP) also inhibited TPA clearance by 60%. Finally, combined preinjection of M6L5 and GST-RAP almost completely abolished reduced liver uptake of TPA and delayed its clearance by a factor of 10. **CONCLUSIONS:** It can be concluded that (1) the mannose receptor and LRP appear to be the sole major receptors responsible for TPA clearance and (2) therapeutic levels of TPA can be maintained for a prolonged time span by coadministration of the aforementioned receptor antagonists.

PMID: 8994415 [PubMed - indexed for MEDLINE]

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(Circulation. 1997;95:46-52.)

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Articles

Antagonists of the Mannose Receptor and the LDL Receptor-Related Protein Dramatically Delay the Clearance of Tissue Plasminogen Activator

Erik A.L. Biessen, PhD; Marco van Teijlingen; Helene Vietsch; Marrie M. Barrett-Bergshoeff; Martin K. Bijsterbosch, PhD; Dingeman C. Rijken, PhD; Theo J.C. van Berkel, PhD; Johan Kuiper, PhD

the Division of Biopharmaceutics, Leiden/Amsterdam Center for Drug Research, University of Leiden (E.A.L.B., M.v.T., H.V., M.K.B., T.J.C.v.B., J.K.), and Gaubius Laboratory, TNO Prevention and Health (M.M.B.-B., D.C.R.), Leiden, The Netherlands.

Correspondence to Dr Ir E.A.L. Biessen, Division of Biopharmaceutics, LACDR, University of Leiden, PO Box 9503, 2300 RA Leiden, The Netherlands.

► Abstract

Background Clinical application of tissue plasminogen activator (TPA) as a fibrinolytic agent is complicated by its rapid clearance from the bloodstream, which is caused by TPA liver uptake. The mannose receptor on endothelial liver cells and the LDL receptor-related protein (LRP) on parenchymal liver cells were reported to contribute to liver uptake.

Methods and Results In this study, we addressed whether TPA clearance can be delayed by inhibiting receptor-mediated endocytosis of TPA. A series of cluster mannosides was synthesized, and their affinity for the mannose receptor was determined. A cluster mannoside carrying six mannose groups (M_6L_5) displayed a subnanomolar affinity for the mannose receptor ($K_1=0.41\pm0.09$ nmol/L). Preinjection of M_6L_5 (1.2 mg/kg) reduced the clearance of ^{125}I -TPA in rats by 60% because of specific inhibition of the endothelial cell uptake. The low toxicity of

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M₆L₅, combined with its accessible synthesis and high specificity for the mannose receptor, makes it a promising agent to improve the pharmacokinetics of TPA. Blockade of LRP by 39-kD receptor-associated protein (GST-RAP) also inhibited TPA clearance by 60%. Finally, combined preinjection of M₆L₅ and GST-RAP almost completely abolished reduced liver uptake of TPA and delayed its clearance by a factor of 10.

Conclusions It can be concluded that (1) the mannose receptor and LRP appear to be the sole major receptors responsible for TPA clearance and (2) therapeutic levels of TPA can be maintained for a prolonged time span by coadministration of the aforementioned receptor antagonists.

Key Words: plasminogen activators • thrombolysis • cluster mannoside • GST-RAP

► Introduction

Tissue plasminogen activator is a serine protease that plays a central role in the fibrinolytic system.^{1 2} TPA converts plasminogen to plasmin, which degrades blood clot-associated fibrin. The fibrin-specific thrombolytic TPA has proved to be a potent drug in several clinical trials.^{3 4 5} Despite its widespread clinical application, the thrombolytic efficacy of TPA is complicated by its rapid clearance from the circulation, and large doses of TPA must be administered.^{6 7 8 9 10} The short plasma half-life of TPA (ranging from 1 minute in rats to about 6 minutes in humans) results from a rapid liver uptake of TPA.^{6 7 8 9 10 11} In vivo studies on TPA have indicated that at least two different hepatic uptake mechanisms are involved in the clearance of TPA from the circulation, because both parenchymal and endothelial liver cells contribute to the liver uptake of TPA.^{7 11 12 13}

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▼ Methods
▼ Results
▼ Discussion
▼ References

The characteristics of the TPA uptake sites on parenchymal and endothelial liver cells differ markedly.^{7 12 14} Uptake by endothelial liver cells is mediated by the mannose receptor, which recognizes the mannose-rich oligosaccharide chain at Asn₁₁₇ of TPA.^{7 11 12 13} The receptor involved in parenchymal liver cell uptake is not unequivocally identified to date.^{7 12 13 15 16 17} In vitro binding studies revealed that TPA may interact with LRP, the asialoglycoprotein receptor,¹¹ and a novel carbohydrate recognition system.^{7 12 13 15 16 17} Warshawsky et al¹⁶ showed that an established LRP antagonist, GST-RAP, reduced the in vivo clearance of TPA. Major efforts have been undertaken to construct TPA variants with prolonged plasma half-lives.^{18 19 20 21 22 23 24 25} ²⁶ To circumvent endothelial cell uptake of TPA via the mannose receptor, deglycosylated TPA variants were developed, and the clearance of these variants was significantly reduced.^{18 19} Alternatively, deletion of the finger and epidermal growth factor domains also resulted in a significant increase of the plasma half-life,^{21 22 23 24 25 26} whereas blockade of the active site of TPA (protease domain) only marginally affected the plasma half-life.^{12 26} However, the benefit

in overall thrombolytic activity of these variants was often too low to justify further development as a thrombolytic drug.

Therefore, we pursued an alternative approach to improve the pharmacokinetics of TPA. We investigated whether the in vivo half-life of wild-type TPA can be prolonged by blockade of its clearance. We devised and synthesized a series of high-affinity ligands for the mannose receptor. Combination of the developed mannose receptor antagonist with an LRP antagonist reduced the liver uptake of TPA strongly and prolonged the plasma half-life of TPA 10-fold.

► **Methods**

Materials

BSA (fraction V), collagenase (types I and IV), and iodogen were purchased from Sigma Chemical Co [^{125}I]NaI (carrier free) and streptavidin–alkaline phosphatase conjugate were from Amersham. Pronase and DNase I were from Boehringer Mannheim GmbH. Nycodenz was from Nycomed Pharma AS (Oslo, Norway). HEPES was from Merck. Recombinant TPA was from Boehringer Ingelheim GmbH. All other chemicals were of analytic grade. The synthesis of M_6L_5 is described in detail elsewhere.²⁷

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Production and Isolation of GST-RAP

A plasmid (pGEX) encoding for a fusion protein (GST-RAP) of GST and the 39-kD protein or receptor-associated protein (RAP), which was transformed in *Escherichia coli* (DH5 α), was a generous gift of Dr J. Herz (Dallas, Tex). GST-RAP was produced exactly as described.²⁸ The potency of GST-RAP to displace trypsin-activated ^{125}I - $\alpha_2\text{M}$ binding from its receptor was essentially equal to values described in the literature (IC_{50} , 1 nmol/L).

Isolation of Human Mannose Receptor

Human mannose receptor was isolated from human placenta after solubilization with Triton X-100 and subsequently purified by affinity chromatography over mannosylated albumin-sepharose according to Otter et al.²⁹

Biotinylation and Radiolabeling of TPA

TPA was dialyzed against 0.1 mol/L NaHCO_3 (pH 8.5) and reacted with *N*-hydroxysuccinimide–activated biotin (Zymed Laboratories Inc) at a ratio of 1 mol TPA to 200 mol *N*-hydroxysuccinimide–activated biotin at room temperature for 3 hours. After reaction, the modified protein was dialyzed against 20 mmol/L Tris buffer, pH 7.4, containing 0.01% Tween-80 (vol/vol).

Recombinant TPA was iodinated by the iodogen method as described, and a specific radioactivity of 3500 to 5000 cpm/ng protein was obtained.⁷

Mannose Receptor Binding Assay

Displacement studies of the binding of biotinylated TPA to isolated human mannose receptor were performed according to the procedure of Otter et al.²⁹ Plates were coated with 100 μ L solubilized receptor in loading buffer (pH 7.4) containing 0.02 mol/L Tris-HCl, 5 mmol/L CaCl_2 , and 0.15 mol/L NaCl at 4°C overnight. Loading buffer supplemented with 0.5% Tween 80 and 0.1% BSA (125 μ L) was added for 30 minutes at room temperature to minimize aspecific binding of ligand to the wells. The receptor-coated wells were preincubated with the indicated amounts of competitor for 30 minutes at room temperature. Biotinylated TPA (1.5 nmol/L) was added and incubated for 2 hours at room temperature. Streptavidin-alkaline phosphatase conjugate was added subsequently, and the wells were incubated for 1 hour at room temperature. Next, *p*-nitrophenolphosphate was added, the wells were incubated for 4 hours at 25°C, and finally the absorption at 405 nm was monitored with a microplate reader. Wells were washed three times with 0.5% Tween-80 in loading buffer supplemented with 0.5% Tween and 0.1% BSA after each step of the procedure. Uncoated wells were used as a control for aspecific binding of biotinylated TPA to uncoated wells.

In Vivo Plasma Clearance and Organ Uptake

Twelve-week-old male Wistar rats (225 to 275 g) were anesthetized by injection with 20 mg pentobarbital IP. The abdomen was opened, radiolabeled TPA (600 μ g/kg body wt) was injected via the vena penis, and at the indicated times, blood samples (0.3 mL) were taken with heparinized syringes from the vena cava and liver lobules were tied off. The liver uptake of the injected compound was corrected for the radioactivity in plasma in the liver at the time of sampling.⁷

Cell Isolation Procedures

For determination of the contributions of different liver cell types to total liver uptake, rats were anesthetized and injected with ^{125}I -labeled TPA via the vena penis. After 10 minutes, the vena porta was cannulated and a liver perfusion at low temperature (<8°C) was started with Hanks' buffer (supplemented with 10 mmol/L HEPES). Parenchymal liver cells, endothelial liver cells, and Kupffer cells were isolated exactly as described.⁷ The contributions of the various liver cell types to total liver uptake were calculated as described.⁷ As found for a number of substrates, no loss of cell-bound label and/or formation of acid-soluble radioactivity occurred during the low-temperature cell isolation procedure, leading to a quantitative recovery of radioactivity associated with the isolated liver cells compared with the total liver association. This was checked for each individual liver cell isolation by comparison of the calculated liver association (from the relative contributions of the various cell types) and the determined total liver association.

Toxicity Studies

Rats (Wistar, male, 250 g) were anesthetized with ether, and PBS (500 μ L) or M_6L_5 (6.0 mg/kg) in 500 μ L PBS was injected in the vena penis. At 2 and 24 hours after injection, blood samples (600 μ L) were taken. Serum levels of alanine aminotransferase, aspartate aminotransferase, and γ -glutamyl transferase were determined enzymatically with Boehringer Mannheim SYS-3

BM/Hitachi 747 enzyme kits. Kinetic determination of lactate dehydrogenase activity in serum was determined on an SYS-3 BM/Hitachi 747 with the Boehringer Mannheim LDH kit. After 24 hours, rats were killed and liver, spleen, and kidney were excised, weighed, and analyzed histologically.

Data Analysis

The displacement binding data were analyzed according to a single-site model with a computerized nonlinear fitting program (Prism, GraphPad Software) to calculate the IC_{50} values.³⁰ The K_i was calculated from the corresponding IC_{50} by the Cheng-Prusoff equation [$K_i = IC_{50} / (1 + \text{Ligand} / K_d)$] and assuming the K_d of TPA to be 1.0 nmol/L. Pharmacokinetic studies of TPA clearance were analyzed according to a two-phase exponential decay model using the same program. Clearance (Cl) was calculated from the area under curve (AUC) of the plasma decay and the injected dose of TPA according to the equation $Cl = \text{Dose} / \text{AUC}$. The significance of differences between means was tested by unpaired two-way Student's *t* test. Significance of the differences in TPA clearance between control and treated rats was analyzed by one-way ANOVA with a Student-Newman-Keuls multiple-comparison post hoc test (Instat, GraphPad software).

► Results

Mannose Receptor Binding Studies

A series of cluster mannosides on a base of an oligolysine backbone was synthesized²⁷ (for chemical structure see Fig 1□). The cluster mannosides contain an increasing number of mannose residues, and their affinity for the isolated human mannose receptor was tested (Fig 2□). All cluster mannosides completely inhibited the binding of biotinylated TPA to the mannose receptor, and the potency to compete for the binding of TPA increased dramatically with increasing mannose valency. From the inhibition curves, the inhibition constants were calculated. It was found that the inhibition constant of M_6L_5 (0.41 ± 0.09 nmol/L), which showed the highest affinity for the mannose receptor, was almost 10^7 -fold lower than that of mannose (4.0 ± 0.6 mmol/L).

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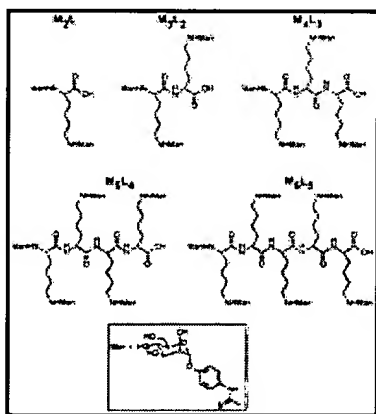
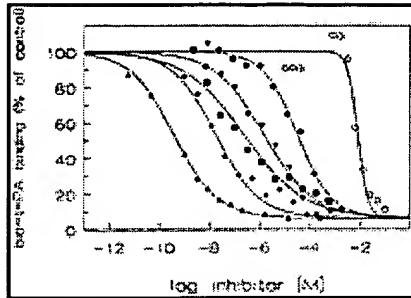


Figure 1. Chemical structures of the synthesized cluster mannosides.

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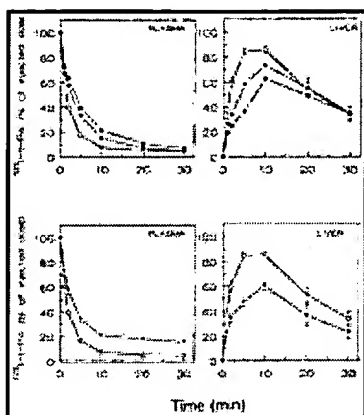
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Figure 2. Displacement of binding of biotinylated TPA to the isolated human mannose receptor by cluster mannosides. Competition experiments were performed as follows. Multiwells coated with isolated human mannose receptor were incubated for 2 hours at 25°C with biotinylated TPA (1.5 nmol/L) in the absence or presence of the indicated amount of displacer: mannose (○), M₂L (●), M₃L₂ (▼), M₄L₃ (■), M₅L₄ (◆), and M₆L₅ (▲). Binding of biotinylated TPA is expressed as percentage of the control binding of biotinylated TPA (without displacer).

Effect of M₆L₅ on the Plasma Clearance and Liver Uptake of TPA

Since TPA is in part cleared from plasma via the liver mannose receptor, we determined the effect of the high-affinity ligand for the mannose receptor, M₆L₅, on TPA clearance. In control rats, ¹²⁵I-TPA (600 µg/kg) was rapidly cleared from the bloodstream (*t*_{1/2}, 1.1±0.1 minutes; Fig 3 □) because of a rapid uptake of TPA by the liver, and a maximum of 86±1.5% of the injected dose was recovered in the liver. Injection of M₆L₅ 1 minute before ¹²⁵I-TPA resulted in a significant and dose-dependent reduction in TPA clearance. At a dose of 0.12 mg M₆L₅/kg, the rate of TPA clearance was reduced by 48% (1.9±0.1 and 3.5±0.2 mL/min for 0.12 mg M₆L₅/kg and controls, respectively; Fig 4 □), whereas 1.2 mg M₆L₅/kg inhibited the clearance for 59% (1.46±0.07 mL/min). Concomitantly, the liver uptake of TPA was delayed, and the maximal liver uptake was reduced to 73±1% and 62.5±1.0% of the injected dose after preinjection of 0.12 and 1.2 mg M₆L₅/kg, respectively.

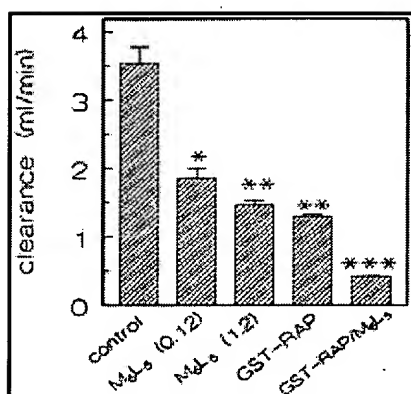
Figure 3. Effect of M₆L₅ or GST-RAP on the plasma clearance and liver uptake of ¹²⁵I-TPA. ¹²⁵I-TPA (600 µg/kg) was injected intravenously into rats that had been preinjected with 0.12 mg/kg M₆L₅ (top, ●), 1.2 mg/kg M₆L₅ (top, ■), 40 mg/kg GST-RAP (bottom, ▼), or PBS (top and bottom, ○). At the indicated times, radioactivity in plasma and liver was determined. Data points are mean±SEM of three (pretreated rats) or eight (control) experiments.



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Figure 4. Effect of mannose receptor and LRP antagonists on the clearance of ^{125}I -TPA. From the plasma clearance data (Figs 3 and 5), TPA clearance (in mL/min) was calculated from the pharmacokinetic parameters area under the curve and injected dose. The level of significance is indicated as * $P < .05$, ** $P < .01$, and *** $P < .001$.

Effect of GST-RAP on the Plasma Clearance and Liver Uptake of ^{125}I -TPA

To address the involvement of LRP in TPA clearance, we studied the effect of an established antagonist of LRP,³⁰ GST-RAP, on the clearance of TPA in the rat. Fig 3 shows that preinjection of GST-RAP (40 mg/kg) strongly affected the pharmacokinetics of ^{125}I -TPA (600 $\mu\text{g/kg}$). At 10 minutes after injection, $21 \pm 1\%$ of the injected dose still resided in the circulation, and the clearance was reduced significantly, by 63% (1.30 ± 0.03 and 3.5 ± 0.2 mL/min for GST-RAP-treated and control, respectively; Fig 4). GST-RAP pretreatment led to a delay in liver uptake of ^{125}I -TPA, and maximal liver uptake was reduced to $60 \pm 2\%$ of the injected dose.

Effect of M₆L₅ and GST-RAP on the Hepatocellular Distribution of TPA

To determine whether the receptor antagonists M₆L₅ and GST-RAP indeed blocked uptake of ^{125}I -TPA via the corresponding receptors, we studied their effects on the uptake of ^{125}I -TPA in

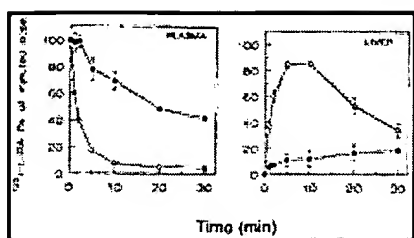
the various liver cell types (Table 1[□]). As described before,⁷ parenchymal and endothelial liver cells appeared to be the major cell types responsible for liver uptake of ¹²⁵I-TPA in control rats; 55±1.5% of total liver uptake of ¹²⁵I-TPA was recovered in parenchymal liver cells, and 40±2% was recovered in endothelial cells. Preinjection of M₆L₅ (1.2 mg/kg) caused a significant shift in the liver cell distribution profile. Parenchymal liver cell uptake increased significantly, to 71±3%, while at the same time the relative contribution of endothelial cells to ¹²⁵I-TPA uptake decreased to 19.5±1% of the total liver uptake. The increase of the relative contribution of parenchymal liver cells was not caused by enhanced uptake per milligram of cell protein. The specific parenchymal liver cell uptake of ¹²⁵I-TPA was not influenced by preinjection of M₆L₅, in contrast to the specific endothelial cell uptake, which was reduced by 72% (124±5% and 430±40% of injected dose/10³/mg cell protein for M₆L₅-treated rats and for controls, respectively).

View this table: **Table 1.** Contribution of Various Cell Types to the Liver Association of ¹²⁵I-TPA: Effect of Preinjection of M₆L₅ or GST-RAP
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By contrast, GST-RAP treatment reduced parenchymal cell uptake by 65% (7.6% versus 21±4% of injected dose/10³/mg cell protein for GST-RAP-treated and control rats, respectively). Concomitantly, specific endothelial cell uptake was increased by 44% to 619% of injected dose/10³/mg cell protein on GST-RAP treatment. Apparently, TPA uptake is partly compensated by an increased uptake by mannose receptor in case the LRP-mediated pathway is blocked. Both GST-RAP and M₆L₅ preinjection did not significantly affect Kupffer cell uptake of TPA.

Effect of Combined Treatment With M₆L₅ and GST-RAP on the Plasma Clearance and Liver Uptake of ¹²⁵I-TPA

These findings demonstrate that although GST-RAP and M₆L₅ both affect TPA clearance, blockade of either receptor system is not sufficient to prevent clearance of TPA. Therefore, we treated rats with both M₆L₅ (1.2 mg/kg) and GST-RAP (40 mg/kg) and determined that the plasma clearance of ¹²⁵I-TPA (600 µg/kg) was almost completely blocked (Fig 5[□]). At 10 minutes after injection, 70±7% of the injected dose is still recovered in the plasma, which is significantly more than in untreated controls (8±0.4%), in M₆L₅-treated rats (21±3%), or in GST-RAP-treated rats (21±1%). The TPA clearance is reduced almost 10-fold, from 3.5±0.2 mL/min for the control rats to 0.42±0.05 mL/min for the combined treatment (Fig 4[□]). Moreover, liver uptake of ¹²⁵I-TPA was almost completely abolished after preinjection with GST-RAP and M₆L₅. Only 18.7±0.8% of the injected dose, at maximum, was recovered in the liver, compared with 86±1.5% for controls.



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Figure 5. Effect of simultaneous preinjection of GST-RAP and M₆L₅ on the plasma decay and liver

association of ¹²⁵I-TPA. ¹²⁵I-TPA (600 μg/kg) was injected intravenously into rats that had been preinjected at 1 minute before TPA injection with PBS (○) or 40 mg/kg GST-RAP plus 1.2 mg/kg M₆L₅ (■).

At the indicated times, radioactivity in plasma and liver was determined. Data points are mean±SEM of three (treated rats) or eight (control) experiments.

To exclude the possibility that the observed effect of combined treatment with GST-RAP plus M₆L₅ on TPA clearance resulted from an aspecific effect of GST-RAP and/or M₆L₅ on hepatic blood flow or receptor-mediated endocytosis in general, we also tested the effect of combined treatment on the *in vivo* kinetics of ¹²⁵I-ASOR, which is an established substrate for the asialoglycoprotein receptor. No effect of combined treatment was observed on liver uptake or plasma clearance of ¹²⁵I-ASOR. The plasma half-life of ASOR was 0.53 minute in treated and 0.51 minute in untreated rats (data not shown).

Toxicity of M₆L₅

To validate the potential of M₆L₅ as a therapeutic additive in thrombolytic therapy, we assessed the acute toxicity of M₆L₅ (Table 2[Ⓢ]). Even at doses (6 mg/kg) 5 to 50 times higher than doses used in this study, M₆L₅ was essentially nontoxic after single bolus injection. Liver, spleen, and kidney weights remained unaffected, and serum parameters for systemic (lactate dehydrogenase) and liver toxicity (alanine aminotransferase, aspartate aminotransferase, and γ-glutamyl transferase) at 2 hours and at 24 hours after injection were essentially unaltered. Histological analysis of liver did not show any signs of toxicity. We may therefore assume that the toxicity of M₆L₅ is very low.

View this table: **Table 2.** Toxicity of M₆L₅ in Rats

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► Discussion

The therapeutic effectiveness of the highly potent thrombolytic agent TPA is reduced by its rapid elimination from the bloodstream, which results from an efficient liver uptake. A first approach to improve the pharmacokinetics of TPA has been the construction of TPA mutants that lack those domains responsible

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for hepatic uptake.^{18 19 20 21 22 23 24 25 26 31 32 33} We used another, still unexplored, approach and developed a highly specific antagonist for the mannose receptor, which is responsible for 40% of the liver uptake of TPA.

▼ References

In search of high-affinity mannose receptor ligands, we synthesized a series of cluster mannosides that contained two (M_2L) to six (M_6L_5) mannose residues per cluster molecule. The cluster mannoside that carried two mannose groups (M_2L ; K_i , 16 $\mu\text{mol/L}$) already displayed a 250-fold higher affinity than α -D-mannose (K_i , 4.0 mmol/L). The most potent mannoside, M_6L_5 , had an affinity for the mannose receptor of 0.41 nmol/L , which is substantially higher than that of ovalbumin (K_i , 290 nmol/L ¹⁴) or mannosylated BSA (K_i , 2.2 nmol/L ³⁴) and quite similar to that of TPA (K_i , 0.6 nmol/L ¹⁴). Previously developed synthetic mannosides—mostly branched oligosaccharides—possessed affinities only in the low micromolar range,³⁵ which is >1000-fold lower than the affinity of M_6L_5 . The subnanomolar affinity of M_6L_5 , in combination with its accessible synthesis, makes M_6L_5 a promising compound to inhibit mannose receptor-mediated uptake of TPA.

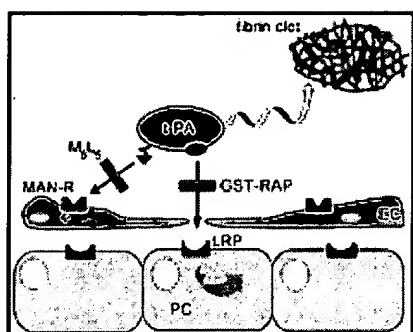
In vivo, M_6L_5 significantly and dose-dependently inhibited the clearance of ^{125}I -TPA (injected at a therapeutic dose of 600 $\mu\text{g/kg}$) by up to 59%. The reduction in liver uptake of TPA by M_6L_5 treatment resulted from a specific inhibition of TPA uptake by endothelial liver cells. This corresponds well with earlier studies showing that the clearance of deglycosylated TPA mutants was retarded by a factor of 3 compared with unmodified TPA.^{18 30 35} Blockade of the plasma clearance of TPA could be reduced 2.6-fold on blockade of the mannose receptor by high doses of mannan (20 mg/kg) or ovalbumin (80 mg/kg).^{7 11} These data illustrate that M_6L_5 is 15- to 70-fold more effective than ovalbumin and mannan in the in vivo blockade of TPA clearance via the mannose receptor. Toxicity studies showed that M_6L_5 is tolerated well at doses 5- to 50-fold higher than the doses that were needed to inhibit TPA clearance. No signs of acute systemic or liver toxicity were observed after single injection of 6.0 $\text{mg } M_6L_5/\text{kg}$. Moreover, M_6L_5 is probably far less immunogenic than mannan or ovalbumin. It can therefore be concluded that the high affinity and specificity of M_6L_5 for the mannose receptor, together with its low toxicity, makes it a valuable therapeutic to improve the pharmacokinetics of TPA.

To establish the involvement of LRP in TPA clearance, we quantified the effect of preinjection of GST-RAP (40 mg/kg) on TPA clearance. GST-RAP, a widely used antagonist of LRP,²⁸ appeared to increase the plasma half-life of ^{125}I -TPA 2.7-fold. Warshawsky et al¹⁶ showed a similar effect of GST-RAP on TPA clearance. In an extension of their study, we show that GST-RAP pretreatment delayed and reduced liver uptake of TPA significantly, by 30%, and the data on the liver cell distribution of TPA show that GST-RAP specifically reduced the uptake by parenchymal liver cells.

The effect of GST-RAP on liver uptake was comparable to that of M_6L_5 . Apparently, neither antagonist can fully block the plasma clearance of TPA or TPA uptake by the liver. The simultaneous blockade of LRP and the mannose receptor by preinjection of GST-RAP and M_6L_5 almost completely abolished liver uptake and at the same time reduced TPA clearance 10-fold. Combined treatment did not affect clearance and liver uptake of another fast-clearing glycoprotein, ASOR, excluding the theory that the blockade of TPA clearance results from aspecific effects of the combined treatment on hepatic blood flow or receptor-mediated endocytosis. The effect of the combined treatment on the clearance of TPA matches very well with the kinetics of TPA reported in rats preinjected with an excess of unlabeled TPA (20 mg/kg).^{7 16} In these studies, half of the injected dose of TPA was still present in the circulation at 30 minutes after injection.^{7 16} Prevention of the liver uptake of TPA by hepatectomy also resulted in a 10-fold decreased clearance.^{6 9 10} Apparently, TPA clearance is prolonged by a factor of 10 by prevention of its liver uptake. Recently, Narita et al³⁶ reported that the plasma half-life of TPA (10 μ g/kg) in RAP-overexpressing mice was enhanced to 20 minutes after preinjection of 150 mg ovalbumin/kg body wt. Although this suggested that the mannose receptor and LRP are the sole contributors to liver uptake of TPA, that was not conclusively established. First, ovalbumin blocks not only mannose receptors but also asialoglycoprotein receptors, which was also suggested to be involved in TPA clearance.¹¹ Second, RAP is a chaperone protein involved in intracellular trafficking of proteins, suggesting that systemic RAP overexpression in mice may also affect other endocytotic pathways that are important for TPA clearance. Most importantly, Narita et al used tracer doses of TPA (10 μ g/kg, which is 60-fold lower than therapeutic doses). At therapeutic doses of 600 μ g/kg, alternative TPA uptake pathways may contribute to TPA liver uptake. This study therefore provides additional information that the mannose receptor and LRP are indeed the only major contributors to the liver uptake and rapid clearance of TPA.

In conclusion, we now show that therapeutic levels of plasma TPA can be maintained for a prolonged time span by blockade of both LRP and the mannose receptor-mediated liver uptake of TPA (Fig 6□). The rather unexplored approach to improve the clinical effectiveness of TPA by means of receptor blockade involves the combined application of the mannose receptor ligands used in this study and TPA-specific LRP antagonists. As a result, lower doses of costly TPA will suffice for thrombolytic therapy, and TPA pharmacokinetics will be greatly improved, leading to fewer unwanted side effects. Blockade of LRP-mediated uptake of TPA by GST-RAP requires rather high doses, which qualifies its potential in thrombolytic therapy. However, more specific and potent LRP antagonists may be developed by combinatorial immunoglobulin repertoire cloning,³⁷ or recently described truncated RAP mutants³⁸ may be applied for this purpose. Compared with application of new slow-clearing TPA variants, application of one of the above antagonists in thrombolytic therapy offers the advantage that it may improve the thrombolytic activity of wild-type TPA, an acknowledged and successful fibrinolytic agent.

Figure 6. Concept for mechanism by which mannose



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receptor and LRP antagonists interfere with TPA catabolism. TPA exposes two domains that interact with mannose receptor on endothelial cells and LRP on parenchymal liver cells, respectively. GST-RAP prevents uptake via LRP, and the newly devised cluster mannoside M_6L_5 prevents mannose receptor-mediated uptake of TPA. Combined therapy totally blocks liver uptake, and subsequently, more TPA is available for the lysis of blood clots. Man-R indicates mannose receptor; PC, parenchymal liver cell; and EC, endothelial cell.

► Selected Abbreviations and Acronyms

α_2M = α_2 -macroglobulin

ASOR = asialoorosomucoid

GST-RAP = fusion protein of glutathione S-transferase and α_2M -receptor-associated protein

LRP = LDL receptor-related protein

M_6L_5 = N^2 -[N^2 -[N^2 -[N^2, N^6 -Tris[N -(p -(α -D-mannopyranosyloxy)anilino)thiocarbamyl]-L-lysyl]- N^6 -[N -(p -(α -D-mannopyranosyloxy)anilino)thiocarbamyl]-L-lysyl]- N^6 -[N -(p -(α -D-mannopyranosyloxy)anilino)thiocarbamyl]-L-lysyl]- N^6 -[N -(p -(α -D-mannopyranosyl-oxy)-anilino)thiocarbamyl]-L-lysine

TPA = tissue plasminogen activator

► Acknowledgments

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